JUL 28 1953

THE CHICAGO MEDICAL SCHOOL
QUARTERLY

VOLUME 14, NUMBER 4

JULY 1953

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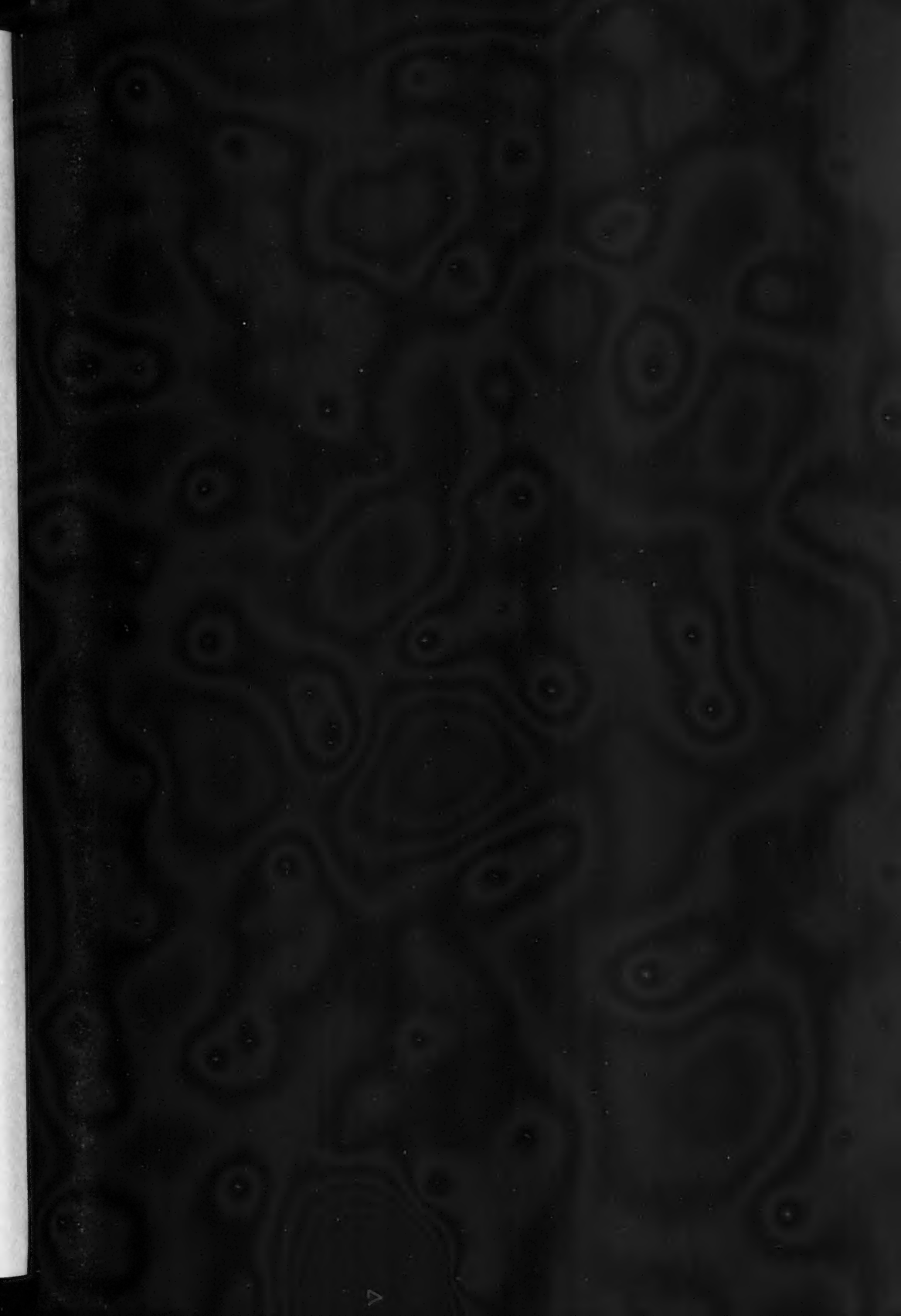

THE CHICAGO MEDICAL SCHOOL
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GLUCAGON: THE ANTI-INSULIN HORMONE OF THE PANCREAS *

PIERO P. FOA, M.D., Ph.D.**

Soon after the discovery of insulin, it was noticed that when crude or "purified" insulin preparations were injected intravenously, their hypoglycemic effect was preceded by a short period of hyperglycemia[1, 2]. This phenomenon was first called the "paradoxic" effect of insulin, then was attributed to undesirable contaminants, and finally to a physiologically active material produced by the pancreas. The name "glucagon" was suggested for this material[3], although the material had not yet been separated from insulin. A few years later, glucagon-free insulin[4] and insulin-free glucagon preparations[5,6] were obtained. Glucagon appears to be more effective when injected directly into the liver via the portal vein than when injected into the systemic circulation[7-9]. In the liver, glucagon brings about glycogenolysis by stimulating the phosphorylase system[10, 11]. The intensity of the hyperglycemic response appears to depend upon the amount of liver glycogen available and is decreased when the glycogen reserves are low, as in prolonged fasting, severe liver disease, or diabetic acidosis[9, 12, 13]. In 1937, on the basis of indirect evidence, Buerger[14] suggested that glucagon might be a hormone capable of mobilizing carbohydrate stored in the liver, making it available for utilization by the peripheral tissues under the effect of insulin. For this reason, Buerger considered glucagon and insulin as synergistic hormones. Glucagon can be found in commercial insulin[15, 16], in the perfusate of normal pancreas[17], in extracts of normal pancreas[18], in extracts of beta cell-free pancreas of alloxan-diabetic dogs[19-22], in the pancreatic blood of alloxan-diabetic dogs[23], in extracts of pancreas after degeneration of the acinar tissue by ligation of the ducts [24-26], and in extracts of the endocrine pancreas of a certain teleostean fish which is free of acinar tissue after destruction of the beta cells with alloxan[27]. These observations rule out the beta cells and the acinar tissue leaving the alpha cells and the connective tissue of the pancreas as possible sites of formation of glucagon. Glucagon can be found also in extracts of gastric mucosa containing alpha-like argentaffine cells[16, 17, 28]. For these reasons, glucagon has been called the "alpha cell hormone"[29, 31]. Glucagon has been held responsible for the high insulin requirement of alloxan-diabetic animals. According to this hypothesis, the alloxan-diabetic animal which lacks beta cells, but has intact alpha cells, is deprived of insulin, but not of its blood-sugar raising antagonist[32]. In contrast, depancreatized animals or men have a relatively low insulin requirement[33, 34], perhaps because they lack both types of cells and, therefore, both hormones. This hypothesis has been criticized[35]. In the absence of any direct evidence

* Presented on April 21, 1953, as one of a series of lectures on "Progress in Endocrinology."

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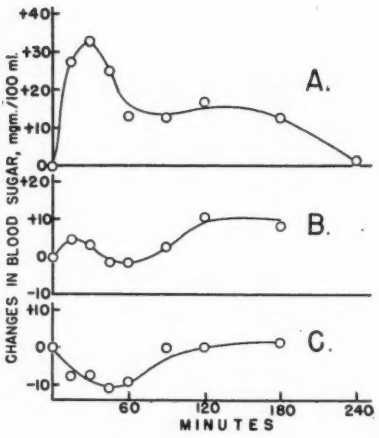

Figure 1

Effect of intravenous injections of extracts of pancreas (A), of cysteine hydrochloride (B), and of saline (C) on the blood sugar of the rabbit.

of the hormonal nature of glucagon and of its secretion by the pancreas in the intact normal animal, Waters[36] refers to glucagon as the "hormone-presumptive", while Conn[37], as late as 1953, states that "the so-called alpha cell hormone may yet prove to be an artifact rather than a normally produced physiologic substance." Glucagon could be a product of a transformation of the insulin molecule caused by some of the drastic steps of insulin manufacture.

The presence of glucagon in crystalline insulin preparations suggests that the two substances have very similar chemical properties which renders their separation difficult. One commonly used method for obtaining insulin-free glucagon consists of inactivating insulin with cysteine[38], or by incubation at pH 10. The glucagon can then be purified by successive alcohol and isoelectric precipitations[8, 16]. Glucagon can be prepared also by using lypohilized pancreas powder as the starting material and liquid ammonia as the solvent[39]. This method avoids all the steps of insulin preparation and uses a solvent known to dissolve many proteins, including insulin, with little or no denaturation and loss of physiological activity[40, 41]. The possibility of causing any cleavage of the insulin molecule with the appearance of hyperglycemic materials is thus minimized. Any insulin found in the liquid ammonia extract can be inactivated by the addition of a calculated amount of cysteine and then glucagon can be partially purified by alcohol precipitation. Glucagon prepared in this manner causes hyperglycemia in the normal rabbit; cysteine and saline do not (Figure 1). Hyperglycemia is caused also by liquid ammonia extracts of stomach (which contains alpha-like cells), but not from the kidney and liver (Figure 2). The action of glucagon extracted from the pancreas with liquid ammonia and of two other glucagon preparations obtained from Eli Lilly and Company was studied using normal and depancreatized dogs. Figure 3 shows that the rise in blood sugar concentration produced by glucagon is much greater in the depancreatized dog controlled with insulin than in the normal animal. Similarly, insulin produced a more marked hypoglycemia in the depancreatized dog than in the normal dog (Figure 4). Thus, the controlled diabetic dog is more sensitive than the normal dog to the action of both glucagon and insulin[13].

On the other hand, when the diabetic animal is deprived of insulin and ketosis develops, the response to glucagon de-

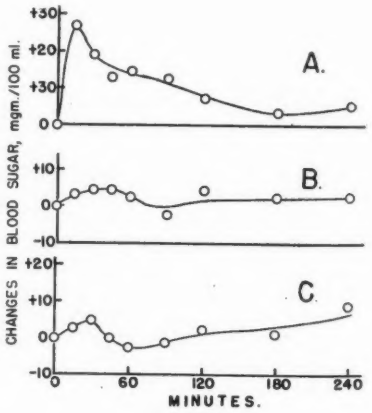

Figure 2

Effect of intravenous injections of extracts of stomach (A), kidney (B), and liver (C) on the blood sugar of the rabbit.

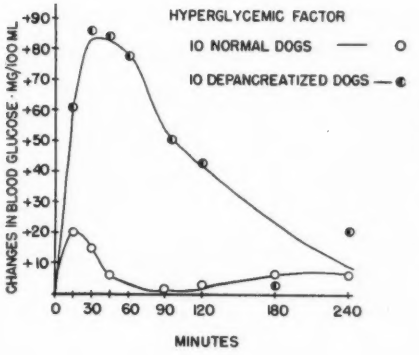

Figure 3

Effect of glucagon on the blood sugar of normal and of depancreatized dogs controlled with insulin.

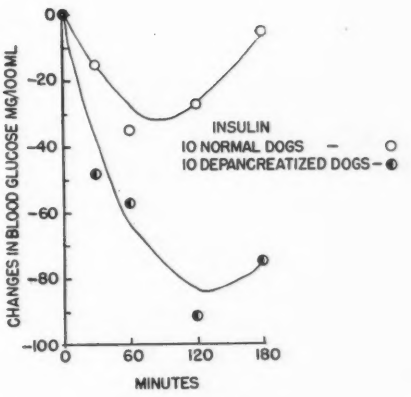

Figure 4

Effect of insulin on the blood sugar of normal and of controlled depancreatized dogs.

creases as the concentration of ketone bodies in the blood increases (Figure 5). Probably both phenomena are the result of the progressive decrease in liver glycogen occurring in decompensated diabetes. A possible explanation for the relatively low sensitivity of the normal animal to glucagon is that the hyperglycemia produced by the injection of glucagon may stimulate insulin secretion just as hyperglycemia produced by the injection of glucose does[23, 42, 43]. Thus in the presence of a normal pancreas, the effect of glucagon would be automatically limited, and only in the depancreatized animal, with a good supply of liver glycogen, could glucagon exert its full action. The observation that insulin hypoglycemia is greater in the depancreatized than in the normal animal agrees with the results of others [44-46] and suggests that, in the normal animal, there may be a reciprocal relationship between the secretion of insulin and the secretion of glucagon. Thus, in the normal animal, insulin hypoglycemia may cause the secretion of glucagon and, in turn, be limited by it; on the other hand, in the depancreatized animal, insulin would be free to show its full effect.

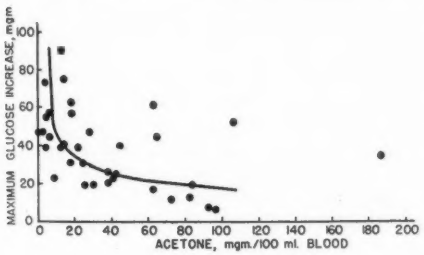

Figure 5

Relationship between the hyperglycemic effect of glucagon and the concentration of ketone bodies in the blood of non-controlled depancreatized dogs.

This homeostatic balance between insulin and glucagon was studied further by means of cross-circulation experiments[47]. In these experiments, the pancreaticoduodenal vein of a donor *dog D* was anastomosed with the femoral vein of a recipient *dog R* (Figure 6). The secretion of insulin or glucagon by the pancreas of *dog D* could thus be detected by the changes produced in the blood sugar of *dog R*[48]. With this technique, it was possible to demonstrate that when glucose is injected into the donor dog, the rise in its blood sugar is followed by a sharp hypoglycemia in the recipient (Figure 7). This suggests that the injection of glucose stimulates the pancreas of the donor to produce insulin (Figure 7). This insulin is then carried by the anastomosis into the recipient dog where it causes a fall in blood sugar. When, in control experiments, the dogs are connected by means of a mesenteric-

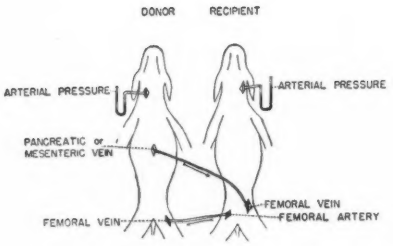

Figure 6

Cross-circulation set-up. The pancreatic (or duodenal) blood of the donor dog flows into femoral vein of the recipient. A return flow is established between a femoral artery of the recipient and a femoral vein of the donor. The pancreatic-femoral anastomosis is open continuously; the return flow only as necessary to keep the blood pressure of the two animals approximately at their initial level. Both dogs are heparinized.

femoral anastomosis, the injection of glucose into the donor dog is followed by a rise in the blood sugar of the recipient because the mesenteric blood of the donor contains glucose, but no insulin (Figure 8). Similarly, when the pancreatic blood is derived from an alloxan-diabetic donor, the injection of glucose into the donor is followed by a rise in the blood sugar of the recipient, as the pancreatic blood contains glucose and, possibly, glucagon, but no insulin. The injection of

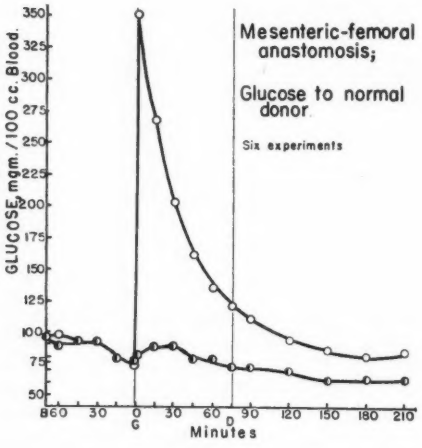

Figure 8

Mesenteric-femoral anastomosis. Symbols as in Figure 7.

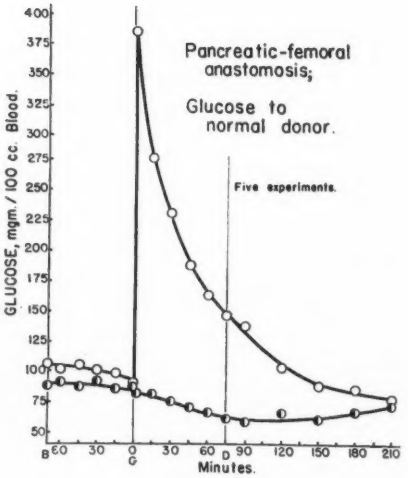

Figure 7

Pancreatic-femoral anastomosis: G: injection of glucose into donor (open circles). D: animals disconnected.

saline fails to produce significant changes in the blood sugar of either dog. The results indicate that the hypoglycemia observed in the recipient dog following the injection of glucose into the donor is the result of an increased insulin secretion brought about by the hyperglycemia. Hyperglycemia can be produced in the donor dog by injecting glucagon instead of glucose. This hyperglycemia, like the hyperglycemia caused by glucose, is followed by a sharp decline in the blood sugar of the recipient dog (Figure 9). The results suggest that glucagon, like glucose, stimulates the pancreas of the donor to produce more insulin. On the other hand, when hypoglycemia is produced in the donor by the injection of insulin, the blood sugar of the recipient increases (Figure 10). This suggests that insulin hypoglycemia in the donor causes the secretion of glucagon which, carried through the pancreatic-femoral anastomosis, in turn causes hyperglycemia in the recipient. When the dogs are connected through a mesenteric-femoral anastomosis, the injection of insulin into the donor is followed by a decrease in the blood sugar of the recipient, presumably because the

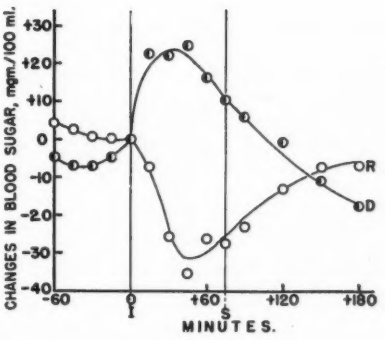

Figure 9

Pancreatic-femoral anastomosis. I: injection of glucagon into donor (D). S: animals separated. R: recipient dog.

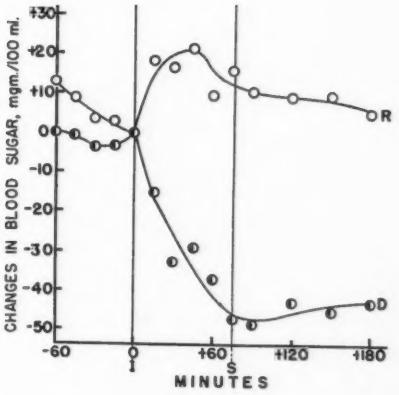

Figure 10

Pancreatic-femoral anastomosis. I: injection of insulin into donor; other symbols as in Figure 9.

mesenteric blood contains some of the injected insulin, but no glucagon (Figure 11).

The hypothesis that glucagon is a true hormone has received support from these experiments. The secretion of this hormone, like that of insulin, appears to regulate and, in turn to be regulated by the concentration of glucose in the blood. In addition, through their effect on blood sugar, insulin and glucagon appear to regulate each other. Thus, when the secretion of glucagon tends to raise the blood sugar, insulin is secreted and lowers it; and when too much insulin is secreted (or injected), glucagon tends to limit its hypoglycemic effect. Glucagon should be considered a physiologic anti-insulin hormone, participating in the maintenance of a normal blood sugar concentration, and acting in a manner similar to that of the anti-insulin hormones of the pituitary-adrenal system[49-50]. Cross-circulation experiments similar to those described above seem to indicate that the secretion of glucagon is stimulated not only by hypoglycemia, but also by the growth hormone of the anterior pituitary[51, 52]. This is one possible reason for the diabetogenic effect of crude anterior pituitary extracts[53, 54] and of purified growth hormone preparations[55.58]. This hypothesis is supported also by the following observations: 1) growth hormone causes a destruction of the insulin-secreting beta cells of the Islets of Langerhans, but leaves the alpha cells. intact[55, 59, 61]; 2) radioactive growth hormone tends to concentrate in the pancreas[62]; and 3) seemingly insulin-free glucagon preparations cause changes in the epiphyseal cartilage of hypophysectomized rats identical to those induced by growth hormone[63]. Recently new tools have been made available for the study of glucagon. The first is a highly purified, insulin-free glucagon prepared by the chemists and biologists of Eli Lilly and Company[64]. The second are certain compounds like diethyldithiocarbamate[65] and cobaltous chloride[66-68] which seem to destroy the alpha cells selectively without injury to the beta cells. These compounds might become

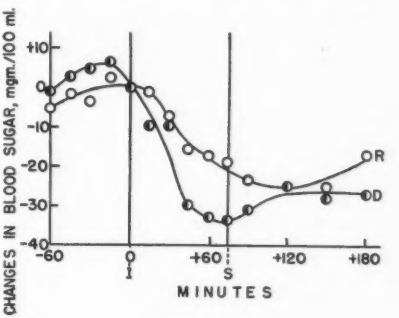

Figure 11

Mesenteric-femoral anastomosis. Symbols as in Figure 10.

as useful for the study of the alpha cells as alloxan has been for the study of the beta cells. Weisberg and Kaplan[69] found that the administration of cobaltous chloride in the rat caused a marked increase in liver and muscle glycogen and suggested that the destruction of the alpha cells may deprive the animal of glucagon and, therefore, decrease the rate of glycogenolysis and spare the glycogen. Much evidence points to the possibility that glucagon may have an important role in clinical medicine and, perhaps, therapy. For example, it has been suggested that an excessive secretion of glucagon may play a role in the pathogenesis of diabetes mellitus [70-73], Kimmelsteil-Wilson syndrome[74], pituitary diabetes[75], carcinoid tumors[76], and certain forms of schizophrenia[77]. On the other hand, an inadequate secretion of glucagon may be present in glycogen storage disease[78-80], "spontaneous" hypoglycemia, and hyperinsulinism[81-83]. It also has been suggested that changes in glucagon secretion may play a role in determining the resistance of diabetic patients to insulin[32, 84-88] and in the so-called diabetogenic effect of insulin[89, 90]. In addition, the glucagon content of commercial insulin preparations may modify their potency and their biological action *in vitro* and *in vivo*[91, 92].

The glycogenolytic effect of glucagon in man has been recently confirmed by means of liver catheterization and peripheral blood sugar determination[93]. The hyperglycemic response to an intravenous infusion has been found decreased after fasting and in patients with hepatitis and cirrhosis and has been suggested as a test of liver function[94]. These are but a few of the problems which must be investigated before the position of glucagon in the family of hormones can be firmly established and before its function in regulating the blood sugar concentration and in maintaining the "steady state" can be fully understood.

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SHOULDER DISORDERS

DONALD S. MILLER, M. D., Ph. D.*

Introduction

The shoulder joint is a complex combination of units—the gleno-humeral, sternoclavicular, acromioclavicular, and scapulo-thoracic joints—that must be carefully and studiously examined for a proper and complete diagnosis. Treatment depends on this evaluation. The dynamics of the shoulder joint form the basis upon which the entire unit functions rhythmically. The anatomy of the bones and joints, ligaments, fascia, muscles, blood vessels, and nerves should therefore be known in order to properly conduct the treatment and realize the prognosis.

In a discussion of shoulder joint disorders, it is important to include not only soft tissue and bony conditions, but also problems that arise outside the shoulder joint proper but which produce symptoms referable to the joint. These include the scalenus anticus syndrome, cervical rib syndrome, costoclavicular syndrome, tumors of the cervical spine, cord, or nerve roots, serum neuritis, rheumatoid and hypertrophic arthritis of the cervical spine, cervical spine discs, and the various types of neuritides. Because of the relative infrequency of these latter problems, they shall not be discussed in this paper.

Soft tissue conditions include the bursitides (calcified or non-calcified bursae or musculotendinous conditions), musculotendinous cuff injuries (supraspinatus, infraspinatus, teres minor, and subscapularis muscle tears), bicipital tendinitis, and adhesive capsulitis (peri-arthritis or "frozen shoulder"). Bone disorders in and around the shoulder include fractures of the anatomical or surgical neck of the humerus, dislocations of the shoulder (with or without fractures of the bone), acromioclavicular joint separations, and fractures of the scapular end of the clavicle or acromion.

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Less frequently, one encounters avulsion tears of the long or short head of the biceps tendon, or the subscapularis tendon, and of the pectoralis major or minor muscles.

Soft Tissue Conditions of the Shoulder

A. Bursitides

Bursitis of the shoulder, or calcareous deposits of the musculotendinous cuff, is the most frequent shoulder condition seen in general practice. It is frequently found in the third, fourth, and fifth decades of life and is more commonly seen in the female than the male. The etiological factors are variable. Trauma may precipitate a dormant condition. The acute stage is characterized by severe pain at the superior-anterior border of the shoulder (superior facet), marked limitation of function of the shoulder joint, muscle spasm, and extreme localized tenderness. In severe cases, the bursal sac may be enlarged and visible. The shoulder is kept at the side throughout the ordeal. X-rays taken in the neutral position and the inverted shoulder position reveal calcifications of various sizes and densities. Treatment for the pain should be immediate. Codeine sulphate (grains ½ to 1), Demerol (100 mg.), or even morphine sulfate may be necessary to control the intense pain. For the first two to three days rest is necessary. This, however, should be replaced by guided motions of the shoulder joint, gravity-free pendulum exercises, and continued physical therapy or roentgen therapy. The latter treatment offers relief in seventy to seventy-five percent of the cases and is both painless and economical. Cortisone, 200 mg. the first day, followed by 100 mg. for the next four to five days, is a good supplementary treatment in this condition.

If these conservative measures fail, exposure of the subdeltoid bursa and careful curettement of the calcium may be necessary. Again, physical therapy, guided motions, and exercises are necessary post-operatively. It is extremely

important to avoid a not infrequent sequel of this problem—namely, the "frozen shoulder." Gout should be considered in cases with intractable, painful calcareous shoulder deposits and should be treated accordingly.

B. Musculotendinous Shoulder Conditions

These injuries include those of the external rotator cuff of the shoulder (supra-spinatus, infra-spinatus, and teres minor muscles), as well as the internal rotator cuff portion (sub-scapularis muscle). Indirect trauma generally produces tears of various types (vertical, transverse, and oblique) and may include one or all tendinous insertions. There is no doubt that degenerative lesions of the musculotendinous cuff (in the aged) and local pathological conditions predispose to these tears. More commonly, they occur in the laboring class, generally in the fourth to fifth decades of life. Strain, traction, or a direct blow to the superior-lateral surface of the shoulder joint often causes this condition. Pain of variable intensity is present at the superior portion of the shoulder joint and is accompanied by limited function of abduction (more severe if a complete tear is present) and complete loss of external rotation. The pain is not as intense as that of acute bursitis. Passive motions, carefully carried through normal ranges, are accompanied by only dull, mild pain. An injection of novocaine (10 cc. of a 1% solution) may relieve the pain, but does not improve shoulder function as it does in acute bursitis. Having established the diagnosis of a tear of the musculotendinous cuff, careful consideration should be given to the general health of the patient (sedentary or active) and to the loss of function. If loss of function is minimal, conservative management with local heat, graduated exercises, and an abduction splint is all that may be necessary. If, however, the tear is more severe, particularly in the young age group, surgical exposure of the rent is necessary to produce anatomical re-position of the torn or attenuated tendon at the attachment to the greater tuberosity of the humerus. Following surgery, an abduction splint should be worn for six to eight weeks, supplemented by heat, passive exercises, and some local massage. Various surgical exposures may be used for this condition (McLaughlin, Codman, Jones or De Palma).

C. Periarthritis or "Frozen Shoulder"

This condition, one of the most common problems seen in orthopedic practice, frequently occurs in association with muscular inactivity. It is usually present in the fourth and fifth decades of life and is more frequent in the female than in the male. It may be associated with a biceps tendinitis, a precursor of this condition, but more frequently arises as an aftermath of an acute sub-deltoid bursitis, local trauma, or a general debilitating disease. Inactivity, following the treatment of a coronary heart condition, frequently produces this problem. This has been called "the shoulder-hand syndrome." Whatever may be its cause, the ultimate end result is a shoulder joint that is fixed and painful, with marked atrophy of the surrounding musculature and varying degrees of limitation of function. A fixation of the scapulo-humeral relationship results, associated with pain during attempts at abduction or rotation of the shoulder joint. Clinically, the shoulder joint appears depressed, atrophy of the infra-spinatus and supra-spinatus muscles occurs, and an associated personality change is noticed in the individual. Somato-psychic conditions not infrequently result from such a long, chronic problem. Depressive states, sleepless nights, weight loss, and poor appetite are associated with the debilitating primary condition. The patient requires careful, diligent, and dynamic treatment. A medical survey is important before treatment is instituted. Proper and carefully guided physical therapy, in the form of passive and active exercises, gentle massage, gravity-free pendulum exercises, and "wall climbing" exercises, is necessary to mobilize the joint. This ultimately reduces the pain. Analgesics before treatment may be necessary; sedation during the evening hours is essential. Cortisone, taken by mouth or injected into the joint, may be tried to reduce fibroblastic activity. Stellate nerve block, given weekly,

may also reduce the reflex irritation seen in the "shoulder-hand syndrome." Although many authors object to manipulation of the joint, this procedure, done with care and caution, may be tried with good end results. An abduction splint, applied immediately following manipulation, or abduction positioning of the arm, following manipulation, is utilized to avoid recurrent adhesions. Physical therapy must be continued for many months in order to obtain a good end result.

D. Bicipital Tendinitis

The biceps tendon, originating at the superior glenoid area and continuing downward in the inter-tubercular sulcus, may be the seat of inflammations, adhesions, or ruptures. The diagnosis is generally made by the location of the pain (anterior shoulder joint, directly over tendon), mild limitation of function, and pain on supinating the forearm. The treatment for this condition, which may be a precursor of adhesive capsulitis, is moist heat to the shoulder joint, proper rest periods, and avoidance of irritation to the tendon by limiting extension or supination of the shoulder joint. If the pain continues and the condition progresses, exploratory operation, with resection of the tendon covering or implantation of the tendon in bone, may be necessary.

Other soft tissue conditions seen are traumatic myositis, traumatic capsulitis, paralysis of isolated muscle groups and intra- and extra-articular infections.

Osseous Conditions of the Shoulder Joint

A. Fractures of the Upper end of the Humerus

Fractures involving the greater or lesser tuberosity of the shoulder joint can be treated simply, if no displacement occurs, by the application of a light-weight "hanging cast" or by a Velpeau dressing. It is extremely important after five to seven days, when hemorrhage and swelling subside, that the shoulder be carefully manipulated in all modalities in order to avoid adhesions, tenosynovitis, or fibrosis in and about the shoulder joint. If wide separation occurs (of the tuberosity), surgical exploration and proper replacement by a screw or staple may be necessary. Occasionally, the musculotendinous insertion retracts a large portion of bone, making surgery essential. Again, careful physical therapy instituted several weeks after surgery is important. Fractures of the surgical or anatomical neck, in good position, may also be treated by a light-weight hanging cast or a plaster cuff cast held snugly to the shoulder joint region by soft bandages. After three weeks, these may be removed and physical therapy instituted. It is not essential to get a complete bony union in this type of fracture before massage and careful manipulation are instituted. If wide separation occurs (except in the aged), open reduction may be necessary to correct position and help healing. Pain may be controlled by analgesics such as codeine (grains ½—1), Demerol (50 to 100 mg.), or morphine sulphate (grains ¼). If severe spasm of muscles accompanies the injury, Tolserol may be given in proper doses. A careful examination for nerve or blood vessel injury is important and should be carefully recorded.

B. Dislocations of the Shoulder Joint

The glenohumeral joint, poorly constructed, is a common site of dislocations. Sub-glenoid dislocations are the most common. The "outstretched hand position" is the usual cause of such acute dislocations. Chronic dislocations may occur through trivial accidents. Epileptics may dislocate a shoulder through muscle spasm during an attack. The head of the humerus causes a rent in the capsule, usually antero-inferior in position. Tears in the glenoid labrum and small fractures are found frequently at the inferior portion of the neck of the scapula. Hemorrhage, edema, and muscle contusion is generally associated with dislocations of the head of the humerus. The shoulder appears "squared off" and the arm is immobile at the side. Severe pain accompanies this condition. General anesthesia is necessary for reduction. The arm is externally rotated carefully, the elbow brought to the mid-line, and the head of the humerus placed in the glenoid cavity. A soft tissue bandage of the Velpeau type holds the head of the humerus in place for five to seven days.

A sling then replaces the bandage and physical therapy is instituted in order to avoid adhesions, scarring, and fibrosis in and about the shoulder joint. Several months may be required for rehabilitation of the joint. Careful and guided motions for this period of time are necessary in order to avoid chronic recurrent dislocations. Proper exercises to improve muscle function are important during this rehabilitative period. Athletics, and particularly competitive athletics, are to be carefully avoided. Any motion requiring abduction or external rotation must be curtailed during healing.

Recurrent dislocations of the shoulder are best treated by reconstructing the anterior portion of the gleno-humeral joint by either the Bankhart operation or the Putti-Platt operation. These operations reinforce the anterior portion of the capsule and produce enough surgical fibrosis to prevent displacement of the head of the humerus. The Nicola operation has been discontinued in many clinics. Immobilization after the reconstruction of the anterior capsule should be maintained for four to six weeks. Careful and guided motion, heat and massage, and passive and active exercises are necessary to strengthen the shoulder and improve function. In the aged, acute dislocations should be treated with a shorter period of immobilization because of the greater possibility of periarticular adhesions. Dislocations of the shoulder joint, more than two or three weeks old, in the aged, are best treated by physical therapy, without attempting to reduce the dislocation. Attempts at reduction invariably result in failure—fracture of the neck of the humerus or scarring, with possible involvement of the peripheral nerves or blood vessels.

C. Acromioclavicular Separations

Acromioclavicular separations are frequently found in industrial accidents as well as in automobile collision injuries. The arm, kept to the side, is the recipient of a traction or avulsion injury, causing separation of this joint. This indirect injury, if severe, may tear the trapezoid and conoid ligaments, causing the outer end of the clavicle to be displaced beneath the skin with marked mobility. Local pain, tenderness, and deformity exist following such a severe separation. Milder separations, in which these two ligaments remain intact, are caused by actual or attenuation tears of the acromioclavicular ligament. Although the deformity is not great, local pain, limited function, and local muscle spasms exist. There is considerable difficulty in abducting and rotating the arm actively. Passive motions, however, can be carried through without much pain. The diagnosis should be made early. To reveal separations, X-rays of both shoulders should be taken with the patient in the upright position and holding ten pound weights in each hand. Mild separations may be treated by the application of a Velpeau bandage and adhesive tape compression of the outer end of the clavicle. Frequent dressings may be necessary. In the more severe displacements, a short spica cast, holding the arm in abduction, with compression by a muslin belt at the outer end of the clavicle reduce the displacement and promote healing in the proper position. Resection of the outer three-quarters to one inch of the clavicle may also be done early, or after several weeks of rest. Another method of treatment is repair of the acromioclavicular ligament by a figure of eight fascia lata sling around the coracoid, followed by a spica cast. A pin through the acromioclavicular joint has been used by many orthopedic surgeons. The best results, however, are obtained by conservative management and the utilization of careful physical therapy. If these measures fail, surgical excision of the clavicle offers the best end result. Pain of a chronic type, weakness of the shoulder joint, and "clicking" noises not infrequently accompany this condition.

Arthritis developing in this joint following trauma may be treated by the local injection of novocaine, X-ray therapy, or resection of the outer three-quarters to one inch of the clavicle.

D. Other Fractures around the Shoulder Joint

Fractures of the outer end of the clavicle or into the acromioclavicular joint may be treated by local adhesive taping,

(Continued on page 181)

INTERFERENCE PHENOMENA BETWEEN INANIMATE AND LIVING AGENTS*

GEORGE J. SCHEFF, M.D., Ph.D.**

Introduction

The possibility of providing protection to the host by chemical or biological "interference" has assumed increasing significance in recent years. The basic idea, however, is by no means new. It appears to have been rediscovered from time to time with some modifications.

The common usage of the term "interference" refers to the interaction of any two agents, whether living or non-living, which are mutually capable of cancelling their functional effects. Consequently, the biological processes affected will maintain a normal balance compatible with life.

Historically, the subject can be conveniently subdivided into three groups: 1) classical interference, or drug antagonism between chemically unrelated structures; 2) metabolic interference between chemical analogues; and 3) virus interference in which living organisms interfere with each other in their action on the host cell.

Classical Interference

Beginning with the first group, it seems fair to point out that Brown and Gulbransen [1] were the first to discover the phenomenon about 30 years ago. They made the interesting observation that the well-known curative effect of Trypaflavin in white mice infected with Trypanosomes was entirely or partially abolished if, prior to its administration, Parafuchsin was given to the animals. Soon thereafter it was learned that Parafuchsin could be replaced by other compounds such as Sodium-thioglycollate. Then, some other agents also were discovered which, in proper combinations, acted in a similar antagonistic manner. [2] In an effort to explain these observations a number of theories have been proposed. Some assumed simple displacement of the participating compounds but failed to furnish conclusive evidence in support of their contention. v. Jancso based his concept on the light sensitivity inducing property of Trypaflavin. He found that after Trypaflavin treatment, the infected mice, as well as the Trypanosomes, became light sensitive; that the Trypanosomes which were pretreated with Parafuchsin were less light-sensitive than those which were exposed to the Trypaflavin alone. v. Jancso, therefore, concluded that the Parafuchsin-treated Trypanosomes — similar to the so-called resistant strains — combined less readily and to a far lesser degree with Trypaflavin. Indeed, he even presented quantitative evidence that in the interference test the Trypaflavin extractable from the Trypanosomes was far less than from the ones exposed only to Trypaflavin. Subsequently, however, for reasons not discussed here, various discrepancies showed up which caused his explanation to be discredited.

In 1935-36 a somewhat different approach was adopted by Hassko and myself. [4] We studied the metabolism of the Trypanosomes directly — anticipating a close correlation between the metabolic activities and the viability of these organisms during interference. The assay was carried out with Trypanosomes derived from four rats of approximately equal weights by bleeding and fractional centrifugation of their blood at about the peak of infection. One of the rats, prior to exsanguination, received no treatment; the second was pretreated with Parafuchsin or Sodium thioglycollate; the third was injected with Trypaflavin or Neosalvarsan; and the fourth animal received in succession (one hour intervals) both treatments as indicated for animals 2 and 3.

As can be seen in Table I, Trypaflavin and Neosalvarsan (IIIa and b) reduced decidedly the oxygen uptake and sugar

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* Presented at a Loyola University Pharmacology Seminar, November 6, 1952.

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RAT NUMBER. WEIGHT (TRYP/RBC)	PRE-TREATMENT	TRYPANOSOMES PER 2.5 CC (IN MILLIONS)	O_2 CONSUMPTION PER HOUR AND PER 1 MILLION TRYPANOSOMES (IN CMM)					SUGAR CONSUMPTION PER 5 HOURS PER 1 MILLION TRYP (γ)
			PERIOD*				Σ	
			1	2	3	4		
EXP. 10								
Ia, 186 GM (1/5.2)	CONTROL	29.7	13.09	7.85	5.25	3.76	29.95	20.00
IIa, 166 GM (1/20)	PARAFUCHSIN (4.9MG)	33.7	10.74	6.65	4.48	3.52	25.39	11.59
IIIa, 219GM (1/11)	TRYPAFLAVIN (6.5MG)	34.5	10.52	4.77	3.08	2.11	20.48	7.99
IVa, 219GM (1/14)	PARAFUCHSIN (5.6MG) + TRYPAFLAVIN (6.0MG)	29.5	11.88	6.53	4.39	3.62	26.42	20.42
EXP. 18								
Ib, 169GM (1/20)	CONTROL	27.8	13.43	8.55	6.36		28.34	21.21
IIb, 159GM (1/15)	NA-THIO-GLYCOLATE (63.6MG)	32.2	13.51	8.31	6.76		28.58	20.75
IIIb, 149GM (1/17.7)	NEOSALVARSAN (6.0MG)	27.9	9.62	4.62	3.35		17.59	8.42
IVb, 150GM (1/17)	NA-THIO-GLYCOLATE (63.6MG) + NEOSALVARSAN (6.0MG)	26.7	12.04	7.00	5.24		24.28	19.93

VESSEL CONSTANTS: I 15.74; II 14.99; III 14.07; IV 14.60ML.
FLUID VOLUME: 2.5ML.
INSET: 0.25ML 7% KOH

Table 1

consumption of the Trypanosomes; Parafuchsin (IIa) had a similar but much smaller effect; and Sodium thioglycollate (IIb) proved innocuous. In both interference sets (IVa and b), the results approached those of the controls (Ia and b). Interpreting our findings, we pointed out that specific topographic sites within the Trypanosome are very likely responsible for the various biological functions and assumed that these sites could be eliminated independently one by one proportionally to the extent of injury inflicted. We also postulated from our findings that the interfering agents react with the same site in the parasite. Clark, a year later (1937), gave a similar explanation of "competitive pharmacological antagonism."

These are only a few of the many attempts which have been designed to solve the problem— they all seem to have contributed to our factual knowledge and have paved the way for impending newer developments.

Metabolic Interference

The second group of observations is concerned with "metabolic interference" or, using modern terminology, with the study of antimetabolites. It all started with the well-known chance discovery of Woods[5] and Fildes[6] in 1940 that p-aminobenzoic acid is a potent antisulfonamide factor (Figure 1). Since then, this observation has been extended to many other compounds, and into various fields of research. Basically, the antimetabolites are believed to act by preventing a structurally related metabolite from combining with its normal reactant in the cell. Consequently a kind of deficiency of the essential metabolite will

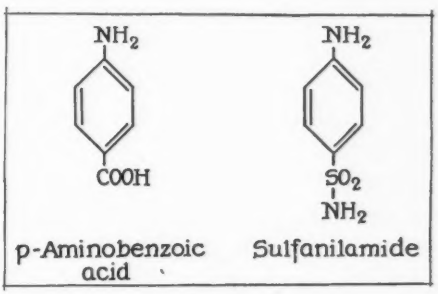

Figure 1

develop. If the reactant is an enzyme, as is so frequently the case, its greater affinity to the antimetabolite will preclude the formation of the normal enzyme-substrate complex. However, it seems established that not only enzymes, but some other agents, antibodies or smaller haptene-like molecules may also behave in a similar way. Although we are still far from understanding all that goes on during these reactions, their practical application, in a number of instances, was highly successful. One of these applications was particularly remarkable since it concerned a premeditated finding. Snyder and his co-workers[7] (1942) found, in the course of routine testing of sulfanilamide derivatives, that these compounds intensified rather than alleviated experimental murine typhus in mice. They inferred by analogy that p-aminobenzoic acid might have the opposite effect and thus control the disease. Experiments verified their contention. Large amounts of p-aminobenzoic acid, when injected or fed to animals, protected them against ten lethal doses of Rickettsial organisms. Beneficial results were also reported in human subjects with clinical typhus fever. However, the large dosage necessary to achieve good results would hardly permit widespread use of the drug since, in higher concentrations, it becomes toxic, and hence would be too dangerous in general practice. Some investigators contended, therefore, that greater selectivity of action should be the primary goal in order to make it more practicable. Others believed that, even though the ensuing deficiency may affect the host as well as the parasite, the parasite will perish first (due to its shorter life span). Once the invader is eliminated, the harm inflicted upon the host could be easily overcome by the administration of a competitive vitamin.

An interesting development took place in connection with the preparation of pantoyltaurine (thiopanic acid), a pantothenic acid analogue (Figure 2). It was found[8] that this compound saves rats from fatal infection with hemolytic streptococci but does not protect mice. This discrepancy was explained when it was found that the level of pantothenic

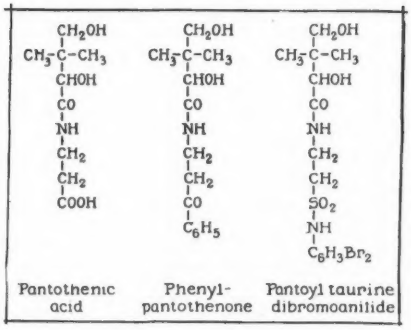

Figure 2

acid in the blood of mice is much higher than in rats. Hence, in mice, the antivitamin effect of pantoyltaurine is quickly neutralized by the natural vitamin. In rats, even with their relatively low concentration of pantothenic acid, excessive amounts of the antivitamin are necessary to produce the desired effect. By painstaking efforts, a series of pantothenic acid analogues have been developed to increase the relative potency of pantoyltaurine. Of these, the dibromoanilide derivative[9] proved the most effective, so that even moderate doses were capable of controlling streptococcal infections induced in mice which could not be coped with previously.

Further progress along similar lines was made through findings in experimental malaria. It was shown that Phenylpantothenone, also a pantothenic acid analogue, is highly active and usually selective in its action.[10] When tried in malaria-infected ducks[11] (avian malaria), it was found to be equal, if not superior, to quinine. In human malaria, it also proved to be effective. However, whether or not such pantothenic acid analogue will replace quinine, time alone can tell.

Recently, some pyrimidine derivatives were also tested for varied purposes (Figure 3). Their study was initiated by the fact that uracil, cytosine, and thymine are parts of the nucleic acid molecule. Since desoxynucleic acids are believed to be implicated in cell division, antimetabolites to any of these pyrimidines would seem therapeutically prom-

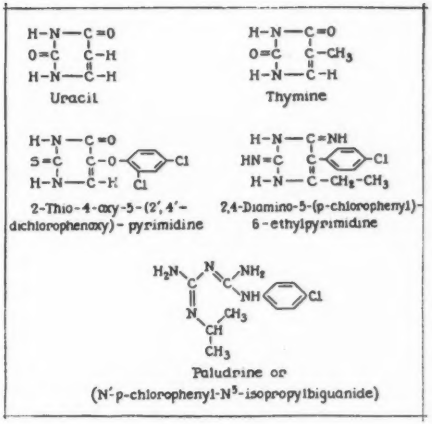

Figure 3

ising. Several hundred such compounds were screened and one in particular, 5 (p-chlorophenyl) 6 ethyl pyrimidine, was found to be most effective. As little as 1 gamma per day sufficed to protect mice against malaria infection (*Plasmodium berghei*)[12]. The toxicity of these pyrimidine analogues is fortunately low enough to permit their introduction into clinical use. Paludrine, a biguanide, has already received universal acclaim in malaria therapy. Furthermore, some of these compounds, *e.g.*, 2 thio-4 oxy 5 (2'4'dichlorophenoxy) pyrimidine, proved effective in virus infections.[13] This seems to be particularly significant since virus infections have not been amenable to treatment up to now.

Also, in the conquest of tuberculosis, some antimetabolites have been introduced therapeutically. Among these, p-aminosalicylic acid (PAS) is outstanding and is usually administered as an adjuvant to streptomycin. It has been established that both drugs together are more efficacious than either drug alone. PAS exerts its specific effect by enzyme inhibition.

The examples presented were limited to anti-infectious studies, although antimetabolites may be operative in many other biological processes.

Virus Interference

The third group is concerned with interference between animal viruses, often referred to as the sparing or blocking effect. It has not escaped the keen observation of older physicians that an individual attacked by one infection may, thereby, become refractory to another one. Jenner, for instance, found, as far back as 1804, that vaccinial lesions failed to develop properly on skin affected by herpetic infections. Similarly, it was recognized in animal experiments that an infection with Yellow Fever virus rendered the animal resistant to Rift Valley Fever virus. However, the significance of these and similar findings was not fully appreciated until recently.

The present interest in this problem originates from two independent investigators. Magrassi[15] observed the interfering effect of encephalitogenic and nonencephalitogenic strains of herpes virus in the rabbit. Hoskins[16] studied the inhibitory effect of neurotropic and viscerotropic strains of Yellow Fever in the monkey. In both instances, the investigated viruses were immunologically related. Subsequently, however, it has been demonstrated that virus interference is not strictly specific, since antigenically unrelated viruses may also interfere with one another. For example, when influenza virus is injected into the brain of mice, its presence will interfere with the development of the St. Louis virus. Henle[17] compiled a complete list of the homologous and heterologous virus combinations exhibiting interference which were known at the time of his publication (Table 2). Since then, these observations have been extended to animal infections with Rickettsiae.[18] It remains to be seen, however, whether the mechanism of interference for the two classes of organisms is the same.

From the various hypotheses which have been advanced to explain the phenomenon, only one has prevailed with relative permanence. It is based on the assumption that virus interference is due to competition for cellular metabolites or enzymes. According to this concept, the interference does not occur during the adsorption of the virus to the receptors on the cell surface (the first stage), but after the virus has entered the susceptible cell (second stage). This idea

INTERFERENCE BETWEEN ANIMAL VIRUSES

HETEROLOGOUS

Rift Valley fever	Yellow fever	Findlay and MacCallum (1937)
Choriomeningitis	Poliomyelitis	Dalldorf *et al.* (1937)
Virus III	Shope fibroma	Andrewes (1940)
W. E. encephalomyelitis	E. E. encephalomyelitis	Schlesinger *et al.* (1943–44)
W. E. encephalomyelitis	Vesicular stomatitis	Schlesinger *et al.* (1943–44)
Mouse encephalomyelitis	W. E. encephalomyelitis	Schlesinger *et al.* (1943–44)
Influenza viruses		Henle and Henle (1943)
		Ziegler *et al.* (1944)
St. Louis encephalitis	W. E. encephalomyelitis	Duffy (1944)
W. E. encephalomyelitis	Influenza	Henle and Henle (1945)
Keratoconjunctivitis	Influenza	Henle and Henle (1945)
Mumps	W. E. encephalomyelitis	Henle and Henle (1945)
Yellow fever	West Nile	Lennette and Koprowski (1946)
Yellow fever	E. enceph. (Venez.)	Lennette and Koprowski (1946)
Papilloma	Sheep dermatitis	Selbie (1946)
Vaccinia	Ectromelia	Andrewes and Elford (1947)
Influenza	Yellow fever	Vilches and Hirst (1947)
Influenza	Rabies	Vilches and Hirst (1947)
Influenza	Semliki Forest	Vilches and Hirst (1947)
Influenza	Newcastle	Ginsberg and Horsfall (1948)

INTERFERENCE BETWEEN ANIMAL VIRUSES

HOMOLOGOUS

Sheep pox	Donatien (1932)
Yellow fever	Hoskins (1935)
Herpes	Magrassi (1935)
Phage	White (1937)
Influenza	Rickard and Francis (1938)
Rinderpest	Pfaff (1938)
Poliomyelitis	Jungeblut and Sanders (1940)
Distemper	Green and Stulberg (1946)
Ectromelia	Andrewes and Elford (1947)
Vaccinia	Dalldorf, Cohen, and Coffey (1947)

Table 2

received its basic support in the work of the Henles [19] and of Isaacs and Edney. [20] The latter, in particular, found (while plotting the hemagglutinin titer versus the challenge virus) that the hemagglutinin titer did not rise uniformly as the concentration of the challenge virus increased. The titer rose slowly at first and then steeply as maximum virus doses were added. They argued [21] that such results could only be obtained when two viruses are competing for the same substance within a cell.

So far, very little is known about the exact nature of these essential substances. Recently, however, by means of an indirect approach, some highly suggestive facts have been disclosed. Horsfall and McCarty[22] were the first to find that the polysaccharide derived from the type B Friedlander bacillus is apt to modify the course of infection in mice inoculated with the pneumonia virus (PVM) or the Mumps virus. The same polysaccharide proved ineffective against the influenza or Newcastle disease (NDV)

virus. This striking difference in behavior has its even more striking counterpart in the reciprocal interference of these viruses. Whereas PVM and mumps viruses do interfere with one another, as do the influenza and NDV viruses, neither group will interfere with the other. Interestingly, the reverse holds true for apple pectin, another polysaccharide, which inhibits the influenza virus and NDV but does not affect PVM or mumps virus.[23] It would seem, therefore, that the growth-inhibiting polysaccharides would somehow control the metabolic pathway required by these viruses. Different viruses apparently use different polysaccharides as their stepping stones in synthesis. If this is the case, interference should be demonstrable in all those instances in which the reciprocal viruses must utilize a common metabolic pathway and compete for a substance essential to both; whereas, if different pathways are used, dual infection rather than interference should result. This thesis is exactly what Horsfall and his colleagues[24] came very close to proving. There are, of course, still a good many problems which require further elucidation. In time, however, the interference phenomenon of viruses will provide a valuable tool in clarifying intracellular processes which could not be studied by any other means.

In conclusion, it may be mentioned that the interference effects have already been applied to a limited extent. This was facilitated by a recent finding that not only fully infective viruses, but agents deprived of infectivity by physical (ultraviolet light) or chemical (formalin) means, are still capable of the blocking effect. This obviously has the great advantage that a properly inactivated virus cannot multiply within the host and hence the exact dosage of virus necessary to ensure blocking can be more accurately administered. Isaacs and Edney[20] reported studies in 1950 in which minimal interfering doses of killed influenza virus were employed to protect against a subsequent live virus infection. Similarly, it may be stimulating to speculate that certain neurotropic viruses may adversely affect or even check the growth of malignancies. For example, vaccine or encephalitis viruses have been shown to inhibit the growth of mouse sarcoma No. 180[25, 26, 27].

Interesting as these findings are, there is no doubt that we are just at the beginning of a new, unexplored field of investigation with rich reward for those who like to toil.

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THE PREOPERATIVE PERIOD FROM THE STANDPOINT OF THE ANESTHESIOLOGIST

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Anesthesiology is one of the fastest growing specialties and there is general agreement that anesthesia today cannot be compared with anesthesia at the beginning of the century. On the other hand, in a very recent paper[1], a nitrous oxide — ether sequence (the two oldest anesthetic agents), is recommended as the best choice of anesthesia for commissurotomy in mitral stenosis, a most delicate procedure that requires superior anesthesia. Thus, obviously the great progress in our field is not primarily due to the new agents at our disposal or the new techniques, important as they are. The progress seems to be due mainly to the devotion and efforts of the anesthesiologist and to a new conception of the importance of maintaining normal physiological conditions in the anesthetized patient. Thus, maintenance of an excellent airway for the patient under the most trying conditions and in the most disadvantageous positions is considered a prerequisite for any anesthesia and does not present a problem today.

The danger of accumulation of carbon dioxide in a depressed patient with decreased tidal exchange has been fully recognized. Satisfactory efforts are made to avoid the deleterious consequences of acidosis by assisting the respiration — increasing the tidal exchange of patients under the effect of depressant drugs or curare or of a patient with an open chest. Recognition of the importance of adequate fluid balance and of the necessity to correct certain untoward effects caused by some positions on the table (*e.g.*, steep Trendelenburg's position in obese individuals[2] or the prone position) helps to prevent shock. The special physiological problems in infants and small children have been widely studied; any resistance to breathing is carefully avoided and dead space is kept at a minimum during anesthesia in children.

Thus, maintenance of normal physiological conditions under anesthesia is mainly the responsibility of the anesthesiologist. The achievement of this goal is directly proportionate to his training, his skill, and his judgment.

But there is a very important part of the anesthetic procedure that commands the attention of the attending physician just as much as the efforts of the anesthesiologist—that is adequate preoperative preparation.

When a patient with a heart ailment is brought to the hospital today for cardiac surgery, the utmost is done to get all the information possible about him and to use all available tests to make a correct diagnosis. Once the diagnosis is made, the effort continues to prepare the patient as well as is humanly possible for the operation. A special heart team is available for this purpose. This preoperative preparation is one of the reasons that cardiac surgery has become a success.

Important and spectacular as cardiac surgery is, it only represents a small part of the surgery that is being performed daily in this country. However, we should be cognizant of the fact that every patient who is undergoing any type of surgery has a better chance of coming through well when he is adequately prepared.

Great progress has been made already. A preoperative blood count and urinalysis is a "must" in every good hospital, as is a thorough physical examination, including a blood pressure reading. Thus it is rare that a blood disease or a severe anemia is overlooked or that a non-controlled diabetic is scheduled for an operation. Thyrotoxic patients are being well prepared and patients with bowel obstruction are decompressed preoperatively. In a patient in shock, every effort is made to restore the circulation before surgery is undertaken. How-

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ever, there are still many instances where things are taken too lightly and where one day more spent in the hospital preoperatively might have made all the difference in the postoperative course of a patient. This one day more might have meant time for an X-ray of the chest in a patient that suffered from a previous "cold"; and that X-ray might have shown an unrecognized virus pneumonia or a tubercular lesion. Increased markings might be discovered and point to a beginning cardiac decompensation. That one extra day might have given time for an electrocardiogram which might have revealed an unrecognized cardiac infarct or some faulty conduction. Any of these findings might have meant a postponement of the operation, time for improvement of the status of the patient, or at least a completely different type of anesthetic management. To give one example: Last week we were approached to select the best method of anesthesia for a patient with a carcinoma of the stomach who was to undergo a gastric resection. We were told that emphysema, chronic bronchitis, and bronchiectasis were present. The surgeon's suggestion was continuous spinal anesthesia . . . a good choice in view of the chest findings. When we saw the patient, however, impaired cardiac status was clinically elicited in this 71 year old man and corroborated by evidence of impaired conduction and left heart strain on an electrocardiogram taken the previous day. Thus, such high spinal anesthesia as is necessary for gastric resection was definitely contraindicated. A paralysis of practically the whole sympathetic system with an ensuing fall in blood pressure could not have been tolerated by this patient. Our choice was "balanced" endotracheal anesthesia, using small amounts of ether to dilate the coronary arteries and frequent suction around and through the endotracheal tube. The patient did very well and is making a satisfactory recovery. I know of another patient, a fifty year old female with a diagnosed duodenal ulcer, visible on X-ray, who complained of increasing and frequent pain in the epigastrium. Diet did not help and surgery was considered. Fortunately, an alert physician found out that the most severe pain occurred after effort, was not related to eating, and had changed in character. An electrocardiogram revealed a recent posterior infarct. The operation was postponed. Imagine the consequences if this patient had been subjected to the stress of this elective operation.

Chest X-rays should be taken in all patients preoperatively and electrocardiograms at least in all patients over forty. This, however, does not mean that physical examination of the patient should be neglected. This should be done very carefully and no details should be overlooked; a thorough preoperative check of reflexes is a necessity in every patient who is to undergo spinal anesthesia. Preoperative histories should be taken with the greatest patience and efficiency; they are invaluable. Anything of importance the attending man has discovered should also be on the chart. Disaster may be prevented by diagnosing a latent glaucoma from the history and by therefore omitting atropine in preoperative sedation. A history of asthma, obtained after careful questioning, changes our choice of premedication (omit morphine) and of anesthesia. We will avoid parasympathomimetic drugs, like pentothal sodium, or histamine releasing drugs, like d-Tubocurarine, which may bring on bronchial spasm and a severe asthmatic attack and greatly diminish the chances for satisfactory recovery.

An unrecognized insufficiency of the adrenal cortex may be followed by severe shock or even death if such a patient is exposed to the strain and stress of even a minor operation. However, if the condition is recognized preoperatively, these patients can be well prepared with cortisone (100 mg. to 200 mg. daily, intramuscularly) and withstand the operation well.

Recently a middle aged Italian woman who did not speak English was brought in for a vaginal hysterectomy. Although a little lethargic, she seemed in good physical condition. On questioning, we learned that several months ago the same operation had been started in a small hospital but that she went into

shock and was unconscious for several hours. The operation had been postponed. There was no history of ACTH or cortisone administration. An electrocardiogram had not been taken at any time. The gynecologist here assumed that there had possibly been a great deal of bleeding during the previous operation. Since the blood count was satisfactory now, and blood for transfusion was prepared, he insisted on starting in spite of the unusual history. Anesthesia was given with great care, excellent oxygenation was present throughout, and adequate fluid replacement was obtained. There was moderate bleeding. The patient did very well. At the end of the operation the patient was awake on the table and the blood pressure and pulse were unchanged. One half hour later, the patient was in shock. She was awake and answered questions rationally, but seemed very restless and full of anxiety. No blood pressure was obtainable and the pulse was weak and fluttery. There was no sign of bleeding. The patient was put in an oxygen tent in moderate Trendelenburg position, but neither that nor the administration of Levophed and more blood changed the picture. Only after intravenous administration of aqueous adrenocortical extract was a normal blood pressure obtained. If the necessary attention had been paid to the previous history and some more facts had been elicited, we could have saved ourselves and the patient some anxious hours by diagnosing and treating a latent insufficiency of the adrenal cortex, which in this case probably was secondary to insufficiency of the anterior lobe of the pituitary.

We are very conscious today of the possibility that temporary insufficiency of the adrenal cortex may be present in a patient coming to surgery. The use of ACTH and cortisone is widespread and, as Lundy and Slocumb[3] pointed out, the insufficiency may become apparent when administration of corticotropin or cortisone is stopped abruptly after having been administered for several weeks. This adrenal cortex insufficiency may be observed from a few weeks to three months after treatment has been stopped. These patients, as well as those who are under cortisone treatment, can be prepared adequately for surgery with 100 to 200 mg. of cortisone intramuscularly daily for two to three days before operation and on the day of surgery. Postoperatively, similar dosage should be maintained for three days. Moreover, aqueous adrenocortical extract should be ready in the operating room to combat possible shock in these patients. Levels of potassium and chloride should be checked so that supplementary potassium chloride can be given if necessary. Patients undergoing an emergency operation under these conditions can be saved by intravenous administration of 50 cc of aqueous adrenocortical extract at the first sign of impending shock. Here, too, knowledge of the fact that the patient received the hormone is invaluable and certainly warrants careful questioning. Every physician should alert his patients to the fact that they are receiving cortisone or corticotropin and that they should tell their surgeon about it in case of an operation, even after the treatment has been discontinued.

One of the most important features of the preoperative preparation is the visit of the anesthesiologist to the patient. Fear of the unknown is a deadly thing. By quiet talk and intelligent explanation, this fear can be destroyed. It gives every patient a feeling of confidence and of being cared for if he can discuss his fears with an expert. Some patients are mortally afraid of receiving spinal anesthesia. If that fear is known, they can be assured in most cases that some other procedure will be chosen. If spinal anesthesia seems the best choice for this patient for this special operation, a quiet talk will make an intelligent patient see things differently. The patient can be assured that he will sleep through the operation and will not hear or see anything in spite of having spinal anesthesia. Another patient, in serious condition, might face the whole procedure with equanimity, but be afraid to see the operating room. He can be told that he will be asleep before being brought to the operating room; his whole outlook

will be changed and he will spend a restful night.

There is more, however, to these preoperative visits. Evaluation of the condition of the patient after careful study of the case enables the anesthesiologist to decide on the anesthetic management and to order adequate preoperative sedation, a major and important part of the anesthetic management. The more we know about the patient, the better will be our choice of the anesthetic management (as pointed out before), and the more perfect will be the preoperative sedation. A patient with latent insufficiency of the adrenal cortex is very sensitive to opiates and barbiturates. Therefore, our preoperative sedation in these patients should be minimal, otherwise we will be faced with a serious depression. A patient with mitral stenosis should get a very small dose of scopolamine in order not to increase the pulse rate. A cyanotic child with Fallot's disease will need a relatively high amount of morphine premedication, so that he will arrive in the operating room quietly, without excitement, and with reduced oxygen requirement. High premedication with opiates is desirable for a thyrotoxic patient; but an old woman with a nontoxic nodule of the thyroid should be sedated sparingly to prevent apnea or respiratory depression, especially when potent anesthetic drugs like cyclopropane are to be used. These are only a few examples to show how premedication has to be individualized and to stress the point that this individualization is possible only after careful study of the patient.

In emergency surgery or in surgery on outpatients, premedication can be given intravenously if the time interval is too short to get the full effect of the prescribed drug after hypodermic injection. Atropine, to minimize secretions in an excited child before ether anesthesia, is very important. It is also important in preparation for sodium pentothal anesthesia — to counteract the parasympathomimetic effects of the drug.

However little time there is before an emergency operation, certain pertinent information concerning the patient has to be obtained. The most important item from the standpoint of the anesthesiologist is to ascertain if the patient has eaten previously. A full stomach before general anesthesia spells catastrophe. Vomiting may occur, followed by aspiration and death. It is hardly believable that some physicians still send children to the hospital for minor operations without instructing the parents not to let them have breakfast that morning. Elective operations in these cases should be cancelled. However, if an emergency operation has to be performed on a patient who has eaten less than four to six hours previously, local block or spinal anesthesia is used if possible. In some instances, analgesia might be administered as during a normal delivery or for incision and drainage of an abscess. In this case the anesthesiologist has to keep in constant contact with the patient to be sure that the patient remains in the stage of analgesia and in possession of active pharyngeal and laryngeal reflexes. If general anesthesia has to be administered, the stomach should be washed out before anesthesia or a cuffed endotracheal tube should be inserted to prevent the possibility of aspiration.

Constant watchfulness is most important. The greater the combined efforts of the referring physician, the surgeon, and the anesthesiologist to know as much as possible about the patient and to convey this knowledge, the better are the chances for the patient. Deficiencies should be detected preoperatively and corrected if possible. Optimum operative conditions should be obtained. Any deficiency that is not corrected preoperatively should be known to the anesthesiologist and taken into account by him when selecting the anesthetic management.

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WHEN SHOULD THE UMBILICAL CORD BE CLAMPED?

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When should the umbilical cord be clamped? With this question as the title of an article, Budin[1], in 1875, then an intern in Paris on Tarnier's service, started a controversy which has become a perennial topic for debate (Pinard — "ligate immediately"; Naegele—"wait until baby cries"). By means of reference to the literature on this subject, some polemics and some personal observation, I hope to lay the controversy at rest with this paper.

The normal physiology of the fetal circulation must be understood to have a clear picture of some of the basic problems involved in this subject. Early in embryonic life, there is a simultaneous development of blood islands and blood vessels on the surface of the yolk sac[2, 3]. Later, capillaries develop in the chorionic villi which ultimately become continuous with the larger vessels of the embryo. The primitive heart acquires contractile powers and a circulation is developed which is a closed system, entirely independent of the mother.

Early in fetal life, the blood volume of the placenta is larger than that of the fetus, but as arterial pressure develops, the blood volume of the placenta diminishes gradually and a certain balance is obtained near term. Just before delivery, the volume of placental blood is just sufficient to supply the requirements of the fetus. By relatively crude methods of draining the blood from the placenta, it has been estimated that the volume of placental blood varies from one-fourth to one-third that of the baby's blood volume[4]. The volume of blood in the newborn has been variously estimated at from ten to fifteen per cent of the body weight. The total blood volume of the placenta and baby is rather constant and is nine per cent of the combined weights[5].

At term, the fetal heart is pumping blood into the hypogastric arteries, thence into the two umbilical arteries and to the placenta. After traversing the capillaries of the chorionic villi, the blood is returned via the umbilical vein to the fetus. At any moment, the volume of returning blood is equal to the volume entering the placenta.

When the baby is born the umbilical cord is clamped and severed. At the moment of birth there is a continuity of fetal conditions for a short time; *i.e.*, the baby is pumping blood into its umbilical arteries to the placenta and blood is flowing into the baby by way of the umbilical vein. The respective quantities of blood are not entirely equal; thus differing from conditions *in utero*. More will be said about this later.

The moment the cord is clamped after birth, there is a quantity of blood remaining in the umbilical vessels and the placenta. This blood is identical with the baby's blood since both were part of the same circulation.

Using the closed system of aspiration such as is employed in blood banks, I have aspirated the blood from placentas after delivery and have found the blood volume to vary within such wide limits as 40 cc. to 150 cc[8]. Other observers have reported comparable results[4,6,7a,b]. Such measurements are necessarily crude. No one has determined the total hematin content of the placenta in order to obtain an accurate total blood volume determination.

The presence of a quantity of perfectly good blood in the placenta and cord, which are finally thrown away, has captured the imagination of many. Therefore, attempts by investigators to utilize placental blood is understandable [9,10,11].

It was shortly after the first trials at using placental blood for transfusions that the question of when to clamp the umbilical cord received added attention. It should be mentioned at this point that the investigators of the use of placental blood made no insistence on a specific time to clamp the cord. The writers who raised this question [4, 7a, 12, 13, 14, 15,

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[16, 17] felt compelled to point out that the placental blood "belongs" to the baby and that by delaying the clamping of the cord the baby "retrieves" or "regains" a certain volume of blood. It was also pointed out that immediate clamping of the cord resulted in a "loss" of blood to the baby comparable to a hemorrhage, thus "depriving" the baby of its placental blood.

The scientific accuracy in the use of such characterizations is open to question. The assumption is made that the fetus supplies the blood to the placenta, whereas it is known[18] that the placenta develops more rapidly than the fetus and has a larger blood volume early in pregnancy which diminishes as the fetus grows. It is probably correct to say that the placenta supplies blood to the baby as it develops; thus, the placenta functions as an organ of nutrition in every conceivable fashion.

Let us compare the human birth with the birth of lower animals such as the horse, cow, dog, or cat. Such comparison is admittedly hazardous. In the lower animal there seems to be no provision made for the offspring to "regain" its placental blood. The cord breaks promptly at birth despite the presence of a quantity of blood in the placenta as high as twenty per cent of the blood volume of the offspring[5].

Assuming that the fetus has supplied blood to the placenta at its hematologic expense, it is understandable that efforts and suggestions should be made to "restore" the placental blood to its owner. This assumption may not be valid. There is no evidence that the fetus has to work for a living. The placenta should not be considered an organ devoid of circulating elements. The placenta and a fortuitous volume of blood are cast off after birth. One should no more bemoan the loss of the blood in the placenta than stress the nutritional value to the baby of the membranes and cotyledons.

The value of blood is being increasingly emphasized. The investigators who advise "returning" the placental blood to its rightful owner claim that, by delaying the clamping of the cord, the baby regains sixty to ninety cc. of placental blood. Some obstetricians[6] advise stripping or milking the cord toward the baby before clamping. That delayed clamping or stripping the cord results in a greater blood volume in the baby has been proved beyond a shadow of a doubt. This fact has bolstered the desirability of a greater blood volume in the baby in the minds of many observers.

There are three methods for proving that the blood volume of the baby is increased by delayed clamping or stripping of the cord:

1. Determination of the blood volume by means of the Evans dye test[14].
2. Measuring the amount of blood in the cord and placenta[4].
3. Weighing the baby before and after delayed clamping[14, 24].

The last two have been the methods most often employed to prove that the volume of the baby's blood is increased by delayed clamping. In examining the studies of many investigators, one is impressed by the marked variability in their results. Though the average of ninety cc. is obtained by most writers, the figures fall into a range of 60 to 120 cc.

It is pertinent to point out various concepts of immediate and delayed clamping. Immediate should mean as soon as the umbilicus appears at the vulva. Certain investigators use the time limit of thirty seconds as immediate. If one opens the clamp on the umbilical cord attached to the placenta, about forty to seventy-five cc. of blood will flow out within thirty seconds. Thus, this element of time is not inconsiderable and may give rise to wide fluctuations in the volume of blood retained in the placenta.

Delayed clamping refers to an elapsed time of ten minutes after delivery[4], although figures ranging from intervals of two to thirty minutes have been reported. It is obvious why numerous inconsistencies are found in the results of placental blood volume determinations.

Williams[6] taught that one should wait until the cord stopped pulsating before

clamping the cord. He probably recognized, and others later proved, that palpating the pulsations in the cord was a convenient way of waiting while blood was flowing into the baby from the placenta. It is clearly understood now that while pulsations of the umbilical arteries are occurring, as much blood is being pumped into the placenta as is leaving by the umbilical vein; that the cord stops pulsating because the arteries go into spasm as the result of cooling of the vessels; that the pulsations farthest from the baby disappear first; and that keeping the cord warm will maintain pulsations.

Accepting the fact that delayed clamping results in a larger blood volume in the baby, one may ask, "How?" The answer is undoubtedly the fact that the uterus, after delivery of the baby, compresses the placenta, forcing blood into the baby. That this compression occurs and increases the venous pressure, can be demonstrated in several ways: 1. If the cord is clamped early, before the placenta is separated, one can see an increase in the turgidity of the umbilical vein as the uterus contracts around the placenta. The turgidity diminishes or disappears as the placenta is delivered; and 2. if one drains the placental blood by way of the cord, one may obtain more blood by manual compression of the placenta.

It was formerly assumed that the respirations of the fetus resulted in aspiration of placental blood. Thus, some investigators have used the onset of respirations as a criterion for clamping the cord. It has been shown that the vascular bed of the lungs of the newborn requires only five per cent of the total blood volume for normal respiration. If the blood volume of a baby is about 300 cc., it will require only fifteen cc. of blood for respiration.

If one accepts the fact that compression of the placenta by the uterus forces blood into the baby, one can deduce the reason for the wide discrepancies in the figures obtained by many investigators for the increase in the blood volume of the baby as a result of delayed cord clamping. The third stage actually begins as the baby is being extruded. Clinical observation has shown that the placenta separates almost immediately after birth[19]. In the process, the placenta is compressed by the uterus. However, the process of separation is frequently altered by many factors, such as oxytocics administered during labor or delivery, analgesia, anesthesia, parity of the patient, and the rapidity of delivery of the baby.

Because of the alteration of the third stage, the vagaries of placental separation and descent into the lower uterine segment or vagina result in variable degrees of placental compression. After determining the blood volumes of more than one hundred freshly delivered placentas[8], I could find no correlation between my findings and the time of clamping the cord. Two examples will clarify one reason for the great discrepancies noted in some writers' findings concerning placental blood volume. A primipara is delivered rapidly with low forceps while under general anesthesia. The uterus, being sluggish, fails to contract and compress the placenta. After ten minutes, the cord is clamped. The placenta is expressed with a blood volume of 120 cc. (delayed clamping). Another patient, a multipara, with the fetal head on the perineum, has Kristellar expression repeatedly applied. An oxytocic is given with the delivery of the anterior shoulder, slow delivery ensues, the cord is clamped immediately, and the placenta is expressed with a blood volume of sixty cc. (immediate clamping). Here we see why immediate clamping may result in the retention of less blood in the placenta than late clamping. The result is a reversal of expected findings.

Under controlled conditions[4], the majority of late cord clampings results in less placental blood. Even in carefully controlled experiments, inexplicable results have been reported. Thus, Ballentine[14] found no correlation between the weight of the baby and the amount of blood "regained" from the placenta, despite the fact that the larger the baby, the larger the placenta and its volume of blood.

I have obtained a greater volume of

blood from large placentas with long cords[8]. The length of the cord is a considerable factor. Some cords contain as much as fifty cc. of blood. While the blood from the cord can flow into the baby readily, the blood from the placenta requires some compression to be forced into the umbilical vein. Where the placenta was suspended still attached to the baby, the increase in the baby's blood volume was only eighty-seven cc. compared to ninety-six cc. in late clampings[14]. This demonstrates that compression of the placenta by the uterus is the important factor in forcing blood into the baby in the late clampings.

The demonstrable increase in the blood volume of the baby as the result of late clamping or stripping has been correlated with certain hematologic and clinical findings in the infant. Some of the more important conclusions include the findings that babies whose cords were stripped had a higher red blood count, a higher hemoglobin, higher initial weight, less weight loss, and less rapid weight loss. Less certain results are: initial birth shock is less; capillaries of the lungs are filled more easily; iron reserve is increased; less demand is made on the blood forming organs of the baby; and less breakdown of proteins occurs[4, 6]. In this work we again find a wide variation in figures. Thus, it is known that capillary or heel blood from the newborn gives higher values than venous blood. Many series of infants were not followed longer than seven days. The following facts were minimized: 1. Forceful stripping of the cord may increase venous pressure and load the circulation to alarming levels[25]; 2. Delayed clamping resulted in higher incidence of physiologic jaundice indicating a possible destruction of excess blood[21]; 3. The role of the spleen in homeostasis[21]; and 4. Delayed clamping cases showed a greater fall of hemoglobin and red blood count the first week of life than did cases having immediate clamping[21].

The weight gains of babies of late and early clampings were parallel the first week[4]. The blood of babies eight to ten months of age who had had immediate clamping of the cord at birth was examined. In these, the red blood count was higher, but the hemoglobin was lower than in those infants who had delayed clamping. This was interpreted as indicative of iron deficiency[4].

Immediate clamping of the cord is indicated under the following circumstances: 1. When the mother is Rh negative. Here the possibility of erythroblastosis fetalis may be present. By early clamping, one prevents sensitized and possibly damaged blood cells from entering the baby's circulation and one may get better results with replacement transfusion, since the blood volume of the baby may be less. 2. When the cord is tight around the baby's neck. 3. When the cord is so short that it retards, prevents, or interferes with the proper conduct of delivery. 4. When the mother or baby requires emergency treatment. 5. When the placenta is incised at the time of cesarean section. Here the baby might lose a critical amount of blood from the cut placental vessels.

Delayed clamping or stripping of cord is recommended by Dieckmann[22] and others when the baby is premature because the volume of placental blood is greater proportionately in premature deliveries. Some pediatricians[27, 28] fail to mention this procedure as important in the prevention of anemia in the premature infant.

McCausland[7b] sent questionnaires to 1,900 certified obstetricians. The questions referred to the time of clamping the cord. The answers indicated no uniformity of practice; about half practiced early clamping. A small percentage stripped the cord.

It is of interest to note that some obstetricians advocate delayed clamping of the cord in the normal case, but express little or no concern for the blood picture of the newborn when the cord is of necessity clamped early.

Summary

On the basis of the data presented, one may deduce the following: Under the exigencies of uncontrolled deliveries of the average obstetric service, babies are born with a variable amount of blood depending principally on the weight of

the baby. Depending on the vagaries of uterine contractions which compress the placenta, a variable amount of blood from the cord and placenta is forced into the newborn before the cord is clamped. Blood examination of numbers of normal newborns reveal wide variations in hemoglobin[26], red blood count, and weight gain or loss. This is normal. Delay in clamping the cord or actively stripping the cord toward the baby usually results in an increase in the blood volume of the baby. The concept that the baby should not be "deprived" of "its" placental blood or that the placental blood "belongs" to the baby has no confirmation. The deliberate increase in the blood volume of the baby by delayed clamping or stripping the cord may be considered a procedure destined to make a normal baby more normal. This procedure may stem from the unconfirmed belief that heavier babies with more hemoglobin are healthier babies. The latitude for blood findings and weights of normal babies is too wide to make such generalizations.

Conclusions

1. In lower animals, such as the dog, cat, sheep, horse, and cow, there seems to be no provision for delay after birth of the animal for the recovery of placental blood. The cord breaks promptly after birth. In the human, there is no evidence that the placental circulation exists at the hematologic expense of the fetus or that the placental blood "belongs" to the baby.

2. Under conditions of the average hospital delivery service, there are wide fluctuations in the amount of blood trapped in the placenta irrespective of early or late clamping of the umbilical cord.

3. Under normal conditions, the blood picture of a newborn reaches its norm within ten days postpartum, regardless of the initial blood findings.

4. In conditions such as tight cord around the baby's neck, cesarean section, and possible erythroblastosis, an immediate clamping of the umbilical cord is indicated; in delivery of premature infants, late clamping may or may not be desirable.

5. In the normal case, it makes no difference to the baby when the umbilical cord is clamped after birth[23].

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CLINICOPATHOLOGIC CONFERENCE

Presented at Mount Sinai Hospital, Chicago, Illinois

DR. I. A. RABENS, Chairman **DR. I. DAVIDSOHN, Secretary**

Abstracted by DR. GERSCHEN SCHAEFER

Clinical History

First Admission: This twenty-nine year old pregnant white female entered Mount Sinai Hospital on May 23, 1952, for evaluation of her renal function. Her physician had discovered the presence of albuminuria on a routine pre-natal examination. She was Rh positive, gravida 2, para 0 and her estimated date of confinement was August 29, 1952. She had had a spontaneous abortion of her first pregnancy at six to seven weeks. On admission, there was a complaint of slight pedal edema and exertional dyspnea. The history revealed migratory joint pains for over one year with swelling of the joints of the fingers and limitation of motion of the fingers. There was no history of any symptoms related to the gastro-intestinal or genito-urinary tracts or the cardio-respiratory system. The blood pressure was persistently normal during this pregnancy.

Physical examination revealed a well-developed, well-nourished white female who was in no apparent distress. Examination of the head and neck revealed no abnormalities except minimal posterior cervical lymphadenopathy. Examination of the lungs was negative. The heart appeared normal in size. The pulse rate was 84 and was regular. The blood pressure was 128/80. No murmurs were heard. Examination of the abdomen revealed the fundus uteri to be seven cm. above the umbilicus. Fetal heart tones were not heard on admission. Pelvic and rectal examinations were deferred. The extremities showed a one plus pedal edema. The finger joints were swollen and tender and there was slight limitation of motion (flexion). The reflexes were normal. After evaluation of the laboratory findings and three blood transfusions for correction of the marked anemia, the patient was discharged on May 29, 1952, in good condition.

Second Admission: The patient re-entered Mount Sinai Hospital on June 17, 1952, with the complaints of dyspnea, orthopnea, and ankle edema for two months.

Physical Examination revealed a well-developed, well-nourished white female who was markedly dyspneic and had a two plus sacral edema. The lungs were clear to auscultation and percussion. There was a grade I systolic murmur at the apex. P_2 was louder than A_2. There was a tumor of pregnancy with the fundus 22 cm. above the pubis. Fetal heart tones were 144 per minute. The liver, spleen, and kidneys were not palpable. There was a four plus pitting edema of the extremities. The blood pressure was 156/80, pulse 140 per minute, and respiration 36 per minute. The patient was treated with packed red cells, Ringer's lactate, 0_2, aminophyllin, Cedilanid, and $NaHCO_3$. She gave birth prematurely to a boy on June 23, 1952. The patient had several reactions to the blood transfusions. Further physical examination revealed a palpable tender mass in the right upper quadrant of the abdomen and a hen's egg sized mass of the left and right adnexae. The patient ran a febrile course. Bronchial breath sounds and a pericardial friction rub were audible in the left chest on July 6, 1952. Shotty post-cervical lymph nodes were palpated on July 13, 1952. Further therapy included vitamins and antibiotics. The patient was discharged on July 19, 1952.

Third Admission: The patient was readmitted on July 25, 1952, with a history of vomiting, weakness, cough, and fever.

Physical Examination revealed a blood pressure of 114/80 and a pulse of 116. Percussion of the thorax revealed flatness in the left lower lobe. Decreased breath sounds were heard in the left base and a pericardial friction rub was audible at the apex. Enlargement of the

LABORATORY DATA

HEMATOLOGY

Blood Counts:	RBC (mill.)	Hb. (Gm.)	C.I.	WBC	Differential Count (in %) Segs	Eos	Lymphs	Stabs	Monos
1st Admission 4/28/52	3.52	7.4	0.94	7,800	83		12		5
2nd Admission 6/17/52	2.91	7.6	0.84	9,950	62	1	7	30	
3rd Admission 7/26/52	2.97	9.6	1.02	3,700	83	1	15	1	
4th Admission 12/9/52	2.96	9.0	0.99	5,350	84		13	1	2

Three plus hypochromia and one plus toxic granulation seen on 4/28/52.
Absolute eosinophil count on 12/9/52 was 11.

Sedimentation rates:	Uncorrected	Corrected
5/24/52 (1st Admission)	71	26
8/28/52 (2nd Admission)	70	32

Peripheral blood: Positive for L-E cells on 8/6/52 and 12/12/52.

Bleeding time: 9 min., 20 sec. on 6/18/52.

Clotting time: 8 min. on 6/18/52.

URINALYSES:	Color	pH	Sp.Gr.	Alb.	RBC	WBC	Sugar	Acetone
1st Admission 5/24/52				4+	4	many	0	0
2nd Admission 6/27/52	straw	5.5		2+	10-12	1-2	0	0
3rd Admission 7/30/52	straw	5.5	1.006	2+	3-4	30-40	0	0
9/23/52	amber	5.5	1.010	3+	3-5	12-15	0	0
4th Admission 12/9/52	amber	5.5	1.012	3+	0	5-10	0	0

BLOOD CHEMISTRY

	Sugar (mg.%)	Urea N. (mg.%)	Creat. (mg.%)	Cl (mEq/L)	Na (mEq/L)	K (mEq/L)	CO_2 (vol.%)	Tot. Prot. (Gm.)	A/G
1st Admission 4/24/52		28.1						6.5	1.4
6/18/52	79	35.8	1.8	122	126	5.8	9	5.7	1.2
2nd Admission 6/20/52		33.6	2.8	107	135	4.9	28		
7/5/52		58.2	2.8	105	132		41	5.1	1.2
3rd Admission 7/29/52								4.3	1.2
8/11/52		116.4	4.0	90	134	7.5		6.3	1.0
4th Admission 12/10/52	100	52.6	3.4	104.1	122	4.7	18.5	5.9	1.6
12/16/52		105.2	6.0	89.7	136	3.6			

Urea Clearance: 16% on 6/18/52.

Uric Acid: 8.0 mg.% on 6/19/52.

Calcium: Total 8.6 mg.%; Ionized 4.7 mg.% on 6/21/52.

Alkaline Phosphatase: 4.4 units on 6/19/52.

Phosphorus: 2.9 mEq/L. on 6/19/52.

Total Bilirubin: 0.08 mg.% on 6/28/52.
Direct Bilirubin: 0.04 mg.% on 6/28/52.

Cholesterol: 285 mg.% on 7/13/52.

SEROLOGIC TEST FOR SYPHILIS: Kline: negative on 12/10/52.

heart to the anterior axillary line was also noted. The patient ran a febrile course and was treated with O_2 and antibiotics. Repeated thoracenteses were performed. With the finding of L-E cells, ACTH was started on August 5, 1952. The patient became disoriented on August 14, 1952, but this subsided under diminished doses of ACTH. The patient was switched to oral Cortisone on August 27, 1952. She developed arthralgias of the fingers and further questioning revealed the occurrence of similar symptoms two years prior to her present illness. An axillary yeast infection was treated with gentian violet. The patient gradually improved and was discharged on a maintenance dose of 37.5 mg. of Cortisone daily on September 27, 1952. The patient was followed in the clinic and did very well on 25 mg. of Cortisone a day, except for a persistent tachycardia, until December 8, 1952, when she was found to have a temperature of 100°F., increased arthralgias, dyspnea, large matted axillary lymph nodes, flatness in both bases, and rales in the right lung to T_4. She was then readmitted to the hospital.

Fourth (Final) Admission: The patient was readmitted on December 8, 1952, with the above symptoms and physical findings. The blood pressure was 190/120. On this admission the patient had a slow downhill course with a pulse as high as 170 and rarely going below 100, despite normal temperatures for the last two weeks of hospitalization. Therapy included ACTH, antibiotics, blood, and parenteral fluids. The patient expired at 10:35 P. M. on December 26, 1952.

Clinical Discussion

Dr. A. Rothman: I saw this patient for the first time when she was about 12 weeks pregnant. She was a para O, gravida II. She had had one miscarriage. When I first saw her, she was rather pale and the only significant laboratory findings at that time were a two plus albuminuria and a red blood count of 2,400,000 with about about 40 per cent hemoglobin. On the basis of these findings, we sent her to the hospital for further studies. At that time, her renal function tests were normal. Her blood chemistry, including urea nitrogen and NPN, were within normal limits. Her blood proteins were normal. She received two or three blood transfusions, after which her blood count picked up and she felt better. But, on a subsequent prenatal visit about three to four weeks later, her blood count was again low and she still ran a persistent albuminuria. She still looked pale and was developing edema of the ankles. At this time, we requested medical consultation. There was a question then whether we were dealing with a toxemia of pregnancy or with some type of renal pathology not associated with toxemia. As an obstetrician, I had the impression that it was not a toxemia of pregnancy. The medical man, on the other hand, maintained that it was a toxemia. The reason I argued against a toxemia of pregnancy was that it was early in pregnancy. Toxemias do occur in the first trimester but they are quite unusual. A severe anemia could not be explained on the basis of toxemia because it is not characteristic of toxemia to produce a profound anemia of this type. The edema and albuminuria would fit in with the toxemia. I believe that on one occasion somebody suspected positive retinal findings. I leaned toward a nephritic process because of the albuminuria and the anemia.

On her second admission, she was admitted with severe dyspnea, orthopnea, and ankle edema and was in profound acidosis. Because of the severe ankle edema, I placed her on ammonium chloride in large doses, around eighty or ninety grains per day. And here is a word of caution: in pregnancy with edema we should be quite sure that the edema is not on the basis of organic renal pathology. If it is, we should use chlorides very cautiously. She had an uneventful premature delivery. The baby was in poor condition and died after a few days. We had hoped that following her delivery she would feel better, as patients with either toxemia or chronic nephritis usually do.

Again a word about pre-eclampsia and chronic nephritis—it is actually not too important in pregnancy to differentiate

between the two. They are both serious conditions. The management is the same for both conditions. It is important to make the differentiation after the patient is delivered, because then we want to know if it is safe for the patient to become pregnant again, or if we should advise against pregnancy. The way to find out is to do renal function tests about six months postpartum. With a pre-eclampsia, renal function will be normal. In chronic nephritis, there will be evidence of renal impairment.

Following her delivery, a mass was palpated in the right upper quadrant. When I examined her I could not feel it. We felt some masses in the lower abdomen. On pelvic examination, I palpated some adnexal masses that were hard, rather irregular, and freely movable. We thought at that time that these represented either calcification of the ovaries or possibly ovarian neoplasm. Operation was not indicated because of her condition and because of the fact that it did not seem to be a malignancy.

Dr. H. Kamin: The first electrocardiogram taken on this patient early in her pregnancy showed a normal pattern. The S-T segments were iso-electric and the T waves were upright. The next graph was abnormal and showed inverted T waves in leads 1, AVL, and V_6. The following graph showed S-T elevations in addition to the inverted T waves. The fourth electrocardiogram was essentially the same as the previous one. The final electrocardiogram showed definite waning of S-T segments and T waves. These findings in the several electrocardiograms showed S-T-T changes which were compatible with a diagnosis of pericarditis.

Dr. M. Shaperman:, The first film was a prenatal chest film. At that time the heart did not seem significantly enlarged. The cardiophrenic sinuses were clear and there was no evidence of an effusion. The lung fields appeared clear. All in all, the film had the appearance of a normal chest.

The next film was taken on July 3, at the time of her second admission. At this time, we noticed a little pleural effusion on the left side. The cardiac silhouette showed a slight enlargement with perhaps a little obliteration of the normal contours, especially down near the apex. The lung fields were still clear. There was a slight degree of interlobar effusion on the left side.

The next film was taken on July 8. That was about the time that the pericardial friction rub was heard. At that time the heart was considerably enlarged and there was a merging of the heart shadow with the pleural effusion on the left side. We thought at the time that we were dealing with a pericardial effusion, because the cardiac contours were lost to some extent. An intravenous pyelogram series showed very poor elimination of the dye, which suggested some impairment of renal function. The liver shadow appeared a little enlarged. In the pelvis, we noted calcifications which had us stumped at the time. We thought they represented some type of adnexal calcification, either fibroid or ovarian. We also entertained the possibility of a dermoid cyst, but we were not too certain.

In a retrograde pyelogram, we noted the calyceal systems on both sides to be fairly normal. The pelves and ureters appeared normal. There was no dilatation to speak of and again we saw calcifications which were outside of the bladder.

The next film was taken about the time of the third admission and again we see this same type of cardiac silhouette, although the pleural effusion has regressed to some extent. The next film was taken on August 5, at about the time ACTH was started. The pleural effusion had increased again, and the cardiac silhouette looked a little larger. During this time, the patient was fluoroscoped and the impression was that we were still dealing with a pericardial effusion because the pulsations were considerably diminished. A film was taken on September 2, after the patient had been on ACTH for a month or so. The pleural effusion had regressed to some extent, although we thought the pericardial effusion was still present. The next film was taken as an out-patient. It showed perhaps a little more regression of the

pleural effusion, but the cardiac silhouette looked just about the same.

A film was taken just prior to the last admission, when rales were heard in the right lung base. We saw a little infiltration in the right base which could be compatible with an early pneumonic infiltration. Effusion was still present to some extent. The last film, taken on the last admission, was rather startling. Again pleural effusion was noted, but it was now bilateral. There was also an interlobar effusion, as well as an infiltrative process in both the right and left lungs, near the periphery. We had a little difficulty in interpreting this last picture. A pneumonitis could produce such findings. This could also be due to a combination of pneumonitis, congestion, and perhaps pulmonary edema.

Dr. M. M. Kirshen: From the clinical point of view, the course of the disease in this patient can be divided into two phases. In the first phase, in which this pregnant woman developed a nephropathy, we were not clear in our minds about the etiology of her condition. She improved after giving birth to a premature child and was sent home for convalescence.

The second phase began two weeks later, when she was readmitted gravely ill with symptoms and signs of a pleurisy and pericarditis.

What was this patient suffering from? Dr. Rothman, who very ably presented the medical aspects of her condition, hospitalized her at the beginning of the fourth month of pregnancy because of severe anemia, albuminuria, and ankle edema. At that time, studies of renal function revealed no abnormalities. There were no changes in her eyegrounds and her blood pressure was not elevated. After a blood transfusion, she was sent home in a relatively good condition. Dr. Rothman had the impression that he was dealing with a chronic nephritis, aggravated by the pregnancy, and he hoped to carry the patient on until the child could be delivered by a cesarean section. Unfortunately, ten days later, the patient had to be readmitted to the hospital because of a severe dyspnea and anuria. When I saw her at that time, in the hospital, it was evident that she was in renal failure. Blood studies revealed a severe electrolyte disturbance (acidosis) and azotemia. When it became known that she was receiving ammonium chloride it was assumed that this therapy, plus poor kidney function, was responsible for the changes in the eclamptic nephropathy or some congefluid intake and a modified Borst treatment restored kidney function in a relatively short time and normalized the electrolyte pattern. After she delivered a premature child without any difficulty her recovery became rapid and she was ready to go home.

I did not agree with the diagnosis of chronic nephritis made by Dr. Rothman. My impression was that we were dealing in this case with an early preeclamptic nephropathy or some congenital abnormality. I was reassured in this assumption by the fact that the patient responded so well to the therapy and improved so rapidly after delivery. The examination of the abdomen after delivery revealed a definite mass in the right upper quadrant, palpated by myself and several other examiners. Intravenous and retrograde pyelograms were negative and the nature of this mass remained uncertain.

A day before the patient was to go home she was suddenly taken ill with chills and fever and developed changes in the left lung which were interpreted as being pneumonia and pleurisy. For a while it was thought that a pericardial rub was heard, but when the patient responded well to antibiotics, the changes in the lung disappeared rapidly, and a chest film was normal, it was assumed that the rub was of a pleuritic nature.

Two weeks later the patient was admitted for the third time with severe chest pain, dyspnea, and high fever. Physical examination revealed pleurisy and pericarditis, and made our alert residents, Dr. Phillips and Dr. Schaefer, think of the possibility of a connective tissue disease. A few days later L-E cells were found in the marrow and peripheral blood. We knew now that we were dealing with lupus erythematosus disseminatus, *sine lupo* (at no time was

a skin lesion present) and that the puzzling nephropathy was the first clinical manifestation of the condition. The tumor mass felt in the right upper quadrant could have been an enlarged gallbladder, which is occasionaliy seen in connective tissue diseases when the blood vessels of that organ become involved.

She was treated with ACTH and Cortisone and after a dramatic course, with many remissions and exacerbations, became stabilized in a fair condition and was discharged to home care and supervised and treated in the out-patient clinic.

Her condition deteriorated slowly and a few months later she was hospitalized again and died in cardiac failure and uremia. Before her death, Dr. Chomet found L-E cells in the peripheral blood smears of the patient. Dr. Hargraves, at the Mayo Clinic, to whom Dr. Chomet sent the slides for verification, believes that this is the first case of proven L-E cells in a peripheral blood smear (Figure 1).

Dr. I. A. Rabens: Was bone marrow examination done to demonstrate the L-E cells?

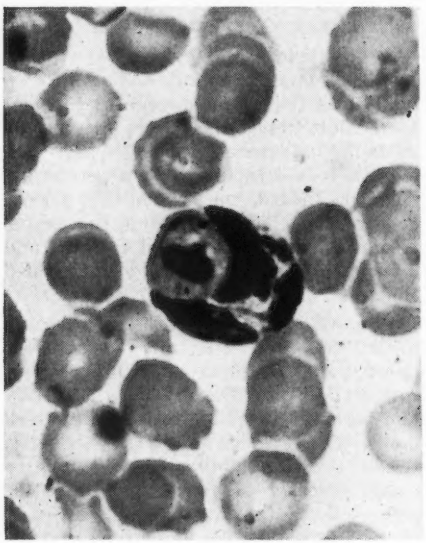

Figure 1

L-E cell in peripheral blood smear.

Dr. M. M. Kirshen: Certainly it was done.

Dr. D. Cohen: I saw this woman on September 4, 1952, and she did have some skin manifestations around her neck, axillae, and gluteal folds. They had been present for two weeks and were quite itchy. It was a simple macular eruption with some thin white scales. My impression was that it had nothing to do with either chronic, discoid, or acute lupus erythematosus. It looked like a fungus and I therefore suggested some scrapings for Monilia. Candida was subsequently isolated and she was treated accordingly.

Dr. S. J. Zakon: I would like to ask the internists what their diagnosis would have been in the absence of the L-E phenomenon? I would also like to emphasize here that lupus erythematosus is not cured by ACTH and/or Cortisone in any given dose for any length of time. These hormones will often prolong life or bring about a remission. These drugs have at most morbidistatic effects. Recently the treatment of lupus erythematosus with atabrine (mepacrine) has been introduced by Francis Page. Acute, subacute, and chronic discoid L-E were treated with atabrine. The effect of atabrine on the skin consists of a change in the color of the skin to variable degrees of yellow or brown. The active L-E lesions become quiescent. The dosage is 100 mg. two or three times daily for a period of five or six weeks. Atabrine may be used concurrently with Cortisone in acute lupus erythematosus. The use of some of the newer antimalarial, non-skin staining drugs had no effect on the lesions of lupus erythematosus.

Dr. G. Schaefer: In retrospect, it is easy to say why the diagnosis wasn't made at this time or that. When one follows the patient from the time of the first admission, when she had a leukocytosis, a normal A/G ratio, and no rash, through an acute acidosis with the presence of red cells, white cells, and even organisms in the urine, you can see how a red herring appeared at every turn. When she first developed pericarditis on the second admission, I suggested

collagen disease, but that is as far as we went. It was on the third admission that one started to think about pleuropericarditis in the presence of a nephropathy and everything seemed to fit together.

Even when this woman was feeling well, with a normal urea nitrogen, normal temperature, and without dyspnea, she ran a constant tachycardia of 120, 130, 140, and as high as 170. With this in mind, I would like to suggest that the autopsy findings will reveal the presence of Libman-Sacks disease.

Dr. I. Davidsohn: First, I would like to make a few remarks about the blood transfusion reactions to which reference was made in the clinical history. The term "transfusion reaction" without further qualification means little, because there are several varieties — febrile, allergic, heart failure, embolic, and hemolytic. The distinction is important for various reasons. The prognosis, the causes, and the treatment are different. In the case under discussion, the transfusions were followed by a so-called febrile reaction, with chills and fever. In a patient like this who already has fever, it may be difficult to ascertain that what seems to be a transfusion reaction is not actually part of the underlying disease. On the other hand, it is known that patients with systemic lupus are prone to react adversely to transfused blood.

Another word of explanation is needed in reference to the statement in the clinical history that L-E cells were found in the peripheral blood. The way the statement is expressed in the history, some special significance might be attributed to this finding. Actually, that is where L-E cells are usually looked for and found at the present time. It is true that bone marrow was used for demonstration of the L-E cells in the original technic as reported by Hargraves. Later, he and others found that it was not necessary to use bone marrow. The so-called L-E phenomenon is the result of a reaction between the plasma of the patient with systemic lupus and leukocytes. It is an immunologic reaction in which a substance in the plasma produces a change in the nuclei of leukocytes and stimulates other leukocytes to ingest this modified nuclear material. (An L-E cell is a leukocyte containing ingested nuclear material.) At the present time, peripheral blood is used for the reaction, with a suitable incubation period. This modification makes the test much simpler than it used to be. The specific substance is in the patient's plasma, but the leukocytes which take part in the reaction do not have to be those of the patient. Leukocytes of any other individual may be used, and even animal white blood cells can be used for the test. The unusual finding in this case was that the phenomenon was observed in a smear of the peripheral blood taken for a blood count — without the usual incubation period. It has been suggested by Dr. Chomet that the patient's agonal condition — with intravascular stagnation of blood, might explain the finding of L-E cells in non-incubated peripheral blood smears. This suggestion needs to be followed up by observations in other terminal cases of lupus erythematosus.

Anatomic Diagnoses

KIDNEYS: Chronic glomerulonephritis; acute necrotizing arteriolitis and glomerulitis; hemoglobinuric nephrosis. HEART: Pericardium: Chronic pericarditis. Endocardium: Atypical verrucous endocarditis (Libman-Sacks disease). Myocardium: Hypertrophy. LUNGS: Pleura: Chronic adhesive pleuritis; bronchopneumonia; edema; chronic passive congestion. COLON: Acute ulcerative colitis. OVARIES: Bilateral calcified fibromas. THYROID: Atrophy. ABDOMINAL CAVITY: Ascites. MUSCLE: Lupus erythematosus. BRAIN: Edema; hyperemia. LIVER, SPLEEN BONE MARROW: Hemosiderosis. LOWER EXTREMITIES: Edema. SKIN (face): Lupus erythematosus. LYMPH NODES: Reactive hyperplasia; lupus erythematosus. ADRENALS: Cortical hyperplasia.

The autopsy findings in the baby: Prematurity (weight 1500 Gm.). BRAIN: Subarachnoid hemorrhage. Cerebellum: Hemorrhage. LUNGS: Bronchopneumonia. No tissue changes suggestive of disseminated lupus.

Figure 2

Adhesive pericarditis with obliteration of pericardial sac. Marked eccentric hypertrophy.

Pathologic Discussion

The heart was considerably enlarged, weighing 620 Gm. The pericardial sac was obliterated (Figure 2). There was diffuse eccentric hypertrophy of both ventricles with thickening of the walls and of the papillary muscles and dilatation of the cavities. The valves showed no abnormalities except for some thickening of the endocardium on the posterior surface of the posterior mitral leaflet and on the adjacent portion of the posterior wall of the left ventricle. This change is the so-called Libman-Sacks atypical endocarditis.

Sections from this area showed degenerative changes in the connective tissue with fibrinoid swelling, giving it a bright red appearance (Figures 3 and 4). This change was seen mainly on the surface and in the ground substance. The collagen fibers were thickened, swollen, and coarse. Vascular changes of several types were seen. In some of the smaller arteries and arterioles there was marked hyperplasia of the walls with narrowing of the lumen (Figures 5 and 6). It must be kept in mind that all these changes are by no means pathognomonic or specific for lupus. Similar changes can be found in other conditions that belong to this group of so-called "collagen diseases," for example, dermatomyositis and scleroderma. Similar hyperplastic vascular changes have also been described in rheumatic fever. The narrowing of the lumen resulting from the hyperplastic change in the wall no doubt interferes with normal blood supply in the corresponding area, with resulting necrosis. This is particularly true when the lumen becomes completely occluded, as in one area seen in this case (Figure 7). Some sections showed the fibrinoid swelling and the degenerative change deep down in the layers of the wall as well as on the surface. This suggests that the fibrinoid swelling is not a surface change but that it is a change in the wall of the heart which has extended toward the surface. One could speculate that this fibrinoid swelling is due to imbibition of plasma components by the tissue due to changes in permeability of the capillaries. Once the plasma gets out of its normal habitat, the circulating blood, the fibrinogen co-

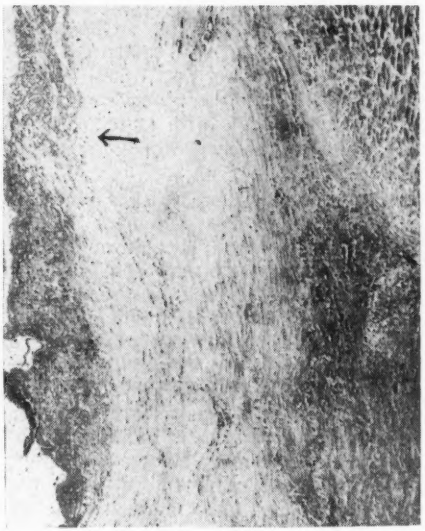

Figure 3

Endocardium: Posterior wall of left ventricle. Libman-Sacks abacterial endocarditis. Fibrinoid degeneration and exudate on surface and in the deeper layers. Degeneration of collagen. x65

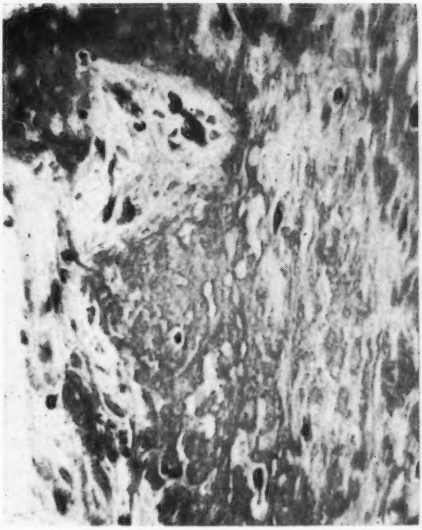

Figure 4

High power magnification of detail in Figure 3 showing fibrinoid degeneration and swelling of collagen in deeper layers beneath the endocardial lining. x350

Figure 5

Hyperplastic and thrombotic changes of small vessels of endocardium of left ventricle. Hydropic degeneration of the thickened endocardium. x60

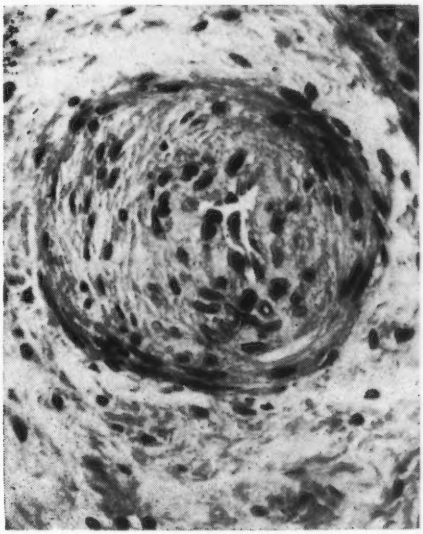

Figure 6

High power magnification of small endocardial vessel in Figure 5, showing extreme thickening of wall and narrowing of the lumen. x650

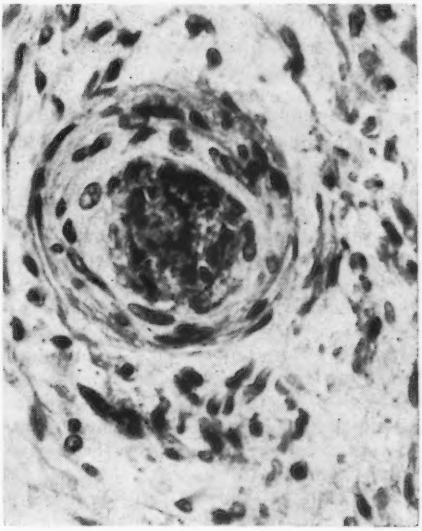

Figure 7

High power magnification of hyperplastic arteriole in Figure 5, showing complete occlusion by thrombus. x800

Figure 8

Skeletal muscle: Hyperplastic changes of vascular wall with occlusion of lumen, surrounded by inflammatory granuloma. x600

agulates and the fibrinoid appearance results.

In the involved area of the myocardium, as well as in many other tissues, especially in the spleen, a great deal of hemosiderosis was present, indicative of the hemolytic process and the resulting hemolytic anemia. This is in keeping with the well-known fact that hemolytic anemia is a common occurrence in disseminated lupus.

Sections from the lungs showed degenerative changes in the walls of the blood vessels of the interalveolar septa. In one somewhat larger arteriole, necrosis of the wall and surrounding infiltration by inflammatory cells, including leukocytes, was seen. Vascular changes of a similar nature were also present in muscle tissue (Figure 8). Similar changes were present in blood vessels in the lymph nodes.

The kidneys showed no significant changes grossly. Microscopic sections showed advanced lesions of a chronic type in the glomeruli. Some capillaries were completely obstructed by fibrous changes resulting in obliteration of the entire glomerulus. In some areas, the glomeruli showed changes compatible with the diagnosis of subacute glomerulonephritis. Some glomeruli were completely necrotic. Actually, practically all forms of renal disease were represented in the kidneys. There were degenerative changes in the tubules which were diagnostic of acute nephrosis. In addition, some tubules showed an absence of epithelium due to necrosis and contents in the lumens characteristic of the so-called hemoglobinuric nephrosis. This lesion was probably caused by shock. In other areas, marked thickening and hyalinization of the wall of the arterioles with focal necrosis was seen, the so-called arteriolar necrosis of malignant nephrosclerosis. The only type of lesion that was absent was the so-called "wire-loop lesion," which is frequently seen in disseminated lupus. However, it is not present in all cases.

The colon showed areas of superficial ulceration and diffuse hemorrhage. Grossly, the picture resembled that seen in uremic colitis. Microscopic sections showed necrosis and inflammatory infiltration of the wall.

Both ovaries were replaced by fibromas and both showed extensive calcification. One of the ovaries, about 6.5 cm. in size, was completely calcified. On microscopic sections there was no evidence of functioning tissue. This finding is of interest in view of the possible role of endocrines in the pathogenesis of disseminated lupus. Some time ago, removal of the ovaries was suggested

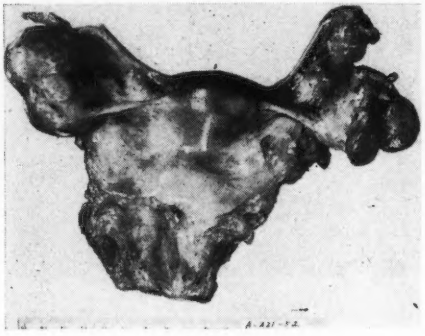

Figure 9

Calcified fibromas of both ovaries.

as a means of therapy. Here, both ovaries seemed to have been eliminated by fibrosis and calcification (Figure 9).

This case permitted us to demonstrate most of the essential pathologic findings in disseminated lupus, except for the so-called "wire-loop" lesions in the kidneys.

In correlating the clinical findings with the autopsy findings, it is probable that the chronic glomerulonephritis is an explanation of the cardiac hypertrophy. The hard mass felt in the pelvis was no doubt due to the ovaries with calcified fibromas.

Clinical pathology of disseminated lupus. There are certain findings in the urine, such as proteinuria, red blood cells, and certain characteristic casts, which make up what is recognized by some as urinary findings characteristic for the disease. It is interesting that in a recent report demonstrating L-E cells in patients with penicillin hypersensitivity, the urine was described as possessing the above mentioned characteristics of lupus. Other findings include retention of non-protein nitrogenous substances, leukopenia, and anemia. The anemia may be hemolytic and in some cases may be associated with auto-immune antibodies. The latter antibodies have been found in some cases studied in our laboratory. Other changes include reversal of the A/G ratio and the occasional presence of cryoglobulin.

The recent studies on the serologic changes in the blood of these patients leading to the discovery of L-E cells are most interesting. The L-E factor responsible for this phenomenon was shown to be of an immune nature. Injection of plasma of a patient with lupus erythematosus having a positive L-E phenomenon produces antibodies in the rabbit that neutralize the L-E factor. Rabbit antiserum produced by injection of normal plasma does not have the spefic neutralizing ability.

REFERENCE

Klemperer, Paul: Pathology of systemic lupus erythematosus, pp. 51-68, *PROGRESS IN FUNDAMENTAL MEDICINE*, Edited by J. F. A. McManus. Lea & Febiger, Philadelphia, 1952.

SHOULDER DISORDERS —

(Continued from page 155)

a sling, and heat. Immobilization should be carried through for from six to eight weeks. Fractures of the scapula may also be treated conservatively by sling, local heat, and careful exercises after muscle spasm ceases. The end result of treatment in both of these conditions is good. This treatment also applies for fractures of the outer end of the acromion.

Conclusions

Disorders of the shoulder joint, therefore, may be divided into problems of the soft tissues and the bony tissues. A careful diagnosis is important to treat the condition properly. A knowledge of the local anatomy and the dynamics of the shoulder joint is essential for the proper evaluation of these problems. The general appearance of the shoulder joint, measurement differences, function of the local musculature, and a careful evaluation of the peripheral nerve and blood supply are essential features in the proper and correct treatment of these shoulder disorders. X-rays, taken in the neutral position and in the inverted shoulder position are essential to localize both articular and extra-articular conditions. Various types of physical therapy, properly given, will alleviate a great deal of the local pain and local spasm and will help the absorption of traumatic edema and local hemorrhage. One should be cognizant of extra-articular problems that may exist and produce symptomatology referable to the shoulder joint.

BOOK REVIEWS

GIFFORD'S TEXTBOOK OF OPHTHALMOLOGY by Francis Heed Adler, M.D. Cloth. Fifth Edition. 488 pages with 281 figures and 26 color plates. Philadelphia and London: W. B. Saunders Company, 1953. $7.50.

This textbook of ophthalmology is specifically designed for the student and general practitioner and places emphasis accordingly. Thus, the sections on hypertension and diabetes have been enlarged in this edition into exceptionally fine discussions which are vital to all practitioners, while the chapter describing the technical aspects of surgery of the eye has been omitted, though an excellent general chapter on the fundamentals of surgery remains. Immediately, one senses the great value in this text. The book is a masterpiece of layout, and thus makes reading easier and more pleasant. It is written in outline form wherever possible, again adding to the accessibility of the material. The illustrations are clear, plentiful, and of great aid. The text material reads smoothly and is thorough where a student or general practitioner would wish and brief where matters become more restricted; yet the text is unquestionably complete within its stated limitations. This is an outstanding text of ophthalmology and is most highly recommended to the student and general practitioner whom the author has chosen to serve.

* * * *

PATHOLOGY: edited by W. A. D. Anderson, M.A., M.D., F.A.C.P. Cloth. First Edition 1453 pages with 1183 illustrations and 10 color plates. St. Louis: The C. V. Mosby Company, 1948. $15.00.

This outstanding textbook of pathology is designed primarily for medical students, yet it covers the field with such thoroughness that it becomes an excellent reference work for all in the field of medicine. Thirty-two well-known and outstanding contributors have written complete discussions of material they have particularly studied, so that each chapter is, in itself, a brief text on a sub-specialty of the field of pathology. The material quoted from the literature is indicated and as a result, the extensive reference at the end of each chapter may be utilized with time-saving foresight. The nearly twelve hundred illustrations are extremely well reproduced and give much meaning to the text. The material is organized with the general principles of pathology discussed first, followed by a discussion of the infectious diseases and the specific organ systems; a sequence which lends itself very well to teaching. In all, this is an excellent and exceptionally thorough volume which will prove highly useful to the beginning student as well as the most advanced practitioner.

TEXTBOOK OF SURGERY by H. F. Moseley, M.A., D.M., M.Ch. (Oxon), F.A.C.S., F.R.C.S., (Eng.), F.R.C.S. (C). Cloth. First Edition. 896 pages with 460 illustrations and 46 color plates. St. Louis: The C. V. Mosby Company, 1952. $15.00.

Dr. G. Gavin Miller, Surgeon-in-Chief of the Royal Victoria Hospital and Chairman of the Department of Surgery of McGill University, in his foreword to this new text describes it as "based on sound principles" and emphasizing "two aspects of teaching, namely, visual aid, and brevity of description." Such remarks clearly indicate that this book has been designed for the student, and, as such, it is an excellent work. For each topic, the text includes a brief mention of the basic sciences, sufficient to provide a good background for the material at hand This is followed by well-summarized discussions of the various disease entities, including symptoms, signs, laboratory work-up, and treatment—surgical and otherwise. The illustrations are outstanding, varying from pencil drawings and clearly reproduced roentgenograms to excellent color photographs and color drawings by Dr. Frank Netter. The contributors to the text are all associated with McGill University and as a result there is close coordination between the various sections, avoiding repetition. In summary, we feel that this textbook is ideally suited for the student and that he will find here a book which has been exceptionally well designed for his needs.

* * * *

THE ANATOMY OF THE NERVOUS SYSTEM: ITS DEVELOPMENT AND FUNCTION by Stephen Walter Ranson, M.D., Ph.D. and revised by Sam Lillard Clark, M.D., Ph.D. Cloth. Ninth Edition. 581 pages with 434 illustrations, 18 in color. Philadelphia and London: W. B. Saunders Company, 1953. $8.50.

This well-known, exceptionally well illustrated book has been revised and brought up to date. One of the most valuable aspects of this revision is the greater blending of structure with function, lending more vitality and interest to the material. Both the basic and clinical material are covered thoroughly. One hundred pages are devoted to sections of the brain, carefully illustrated and neatly described and explained. Important references are noted directly in the text, and thus the book is also of value as a ready source of the important literature in the field. The logical approach, the constant emphasis on the dynamic rather than the static, and the excellence of the abundant illustrations further reinforce the great value of this text. It remains an outstanding work in the field of neuroanatomy and once again is recommended especially to the student as a well written, thorough, and interesting textbook of neuroanatomy.

A MANUAL OF CLINICAL ALLERGY by John M. Sheldon, M.D., Robert G. Lovell, M.D., and Kenneth P. Mathews, M.D. Cloth. First Edition. 413 pages with 27 figures. Philadelphia and London: W. B. Saunders Company, 1953. $8.50.

This textbook is designed for the physician who is interested in doing work in the field of allergy, yet its value as a text for the student or general practitioner is undeniable. Sections covering such aspects of allergy as pollen and mold identification, the preparation of testing and treatment extracts, and office planning for the practice of allergy are clearly designed for the specialist. On the other hand, there are excellent sections on the immunological aspects of allergy, the more common proven allergic clinical entities, the endocrine aspects of allergy, vascular allergy, and collagen diseases, all of which are of interest to everyone. These aspects are covered thoroughly and the authors' discussions are well organized and well written. This text is of obvious value to the allergist, but is also of great value to the student and general practitioner for whom it serves as a thorough and current work.

AMERICAN POCKET MEDICAL DICTIONARY. Paper. Nineteenth Edition. 639 pages. Philadelphia and London: W. B. Saunders Company, 1953. $3.25 plain; $3.75 with thumb-index.

This pocket-sized dictionary is not designed to replace the standard dictionary, but through its emphasis on simplicity and immediate usefulness it has become a valuable dictionary for both students and practitioners. The definitions are exceptionally clear despite their brevity, and the key to pronunciation is easy to follow. Included are concise tables covering such material as arteries, muscles, nerves, and bones which tabulate the most important data concerning each. The dictionary is one of the finest of its type, and is recommended to pre-clinical students, especially, as a handy tool with which one may look up new words as soon as they are introduced in class, leaving more detailed follow-up for later. The dictionary is also of great value for the practitioner's desk where it will serve as a time-saving means of looking up quickly needed terms.

ABSTRACTS SECTION

FOA, PIERO P., H. R. WEINSTEIN, J. A. SMITH, and M. GREENBERG (*Dept. of Pysiol. and Pharm.*). Effects of Insulin on Phosphorylation and Dephosphorylation in Liver Homogenates of Normal, Thiamine Deficient, and Alloxan-Diabetic Rats. Arch. Biochem. and Biophys. *40* (2): 323-333. 1952.

Neuritis is a frequent complication of diabetes mellitus and one which is especially difficult to control. Although it appears to be very similar to neuritis due to thiamine deficiency, it does not respond to thiamine therapy and the best method for its treatment seems to be a painstaking control of the diabetes itself. Experiments were performed to investigate the hypothesis that in diabetes, thiamine is not properly phosphorylated and therefore utilized, so that thiamine deficiency may occur even in the presence of an abundant supply of the vitamin.

Normal rat liver contains about 10 μgm. of thiamine per gram of fresh tissue, more than 80% phosphorylated; thiamine-deficient rat liver contains an average of 2.4 μg. thiamine per gram of fresh tissue, more than 85% phosphorylated; livers from well-fed, alloxan-diabetic rats contain a normal amount of thiamine, which is only 36% phosphorylated. Normal and thiamine-deficient rat liver homogenates split thiamine phosphate during incubation; this dephosphorylation is reversed by thiamine. Incubation does not decrease the thiamine phosphate of alloxan-diabetic homogenates which is already low; addition of thiamine causes an increase in thiamine phosphates. Insulin, like thiamine, reverses thiamine dephosphorylation in normal and thiamine-deficient homogenates, and causes thiamine phosphates to return toward, but not above, the pre-incubation values. In these homogenates, the effects of insulin and thiamine are not additive. Insulin, added to alloxan-diabetic homogenates, increases the thiamine phosphate fraction to values greater than those found before incubation; the increase is greater if thiamine is also added. Under no circumstances have more thiamine phosphates been obtained than are found in normal, non-incubated liver homogenates. Changes in rates of thiamine phosphorylation are not accompanied by changes in oxygen consumption. The results are consistent with the hypothesis that the phosphorylation and utilization of thiamine are below normal in diabetes and are increased by insulin.

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HURWITZ, PAUL (*Asst. Prof. of Ophth.*). Prophenpyridamine Maleate (Trimeton Maleate) in Ocular Allergy, EENT Monthly, V. 31, No. 5, pp. 251-254, May, 1952.

Many diseases of the eye, considered due to other causes, are now known to be allergic. All structures of the eye are subject to allergy, though the most commonly involved are the skin and conjunctiva of the lids. Hypersensitivity of the eye may be induced by contactant or inhalant allergens, ingested proteins, or bacterial toxins.

The treatment of ocular allergies consists of elimination of the offending allergens, desensitization, and adjuvant therapy. The recent advent of adrenocorticotropic hormones, cortisone, and the antihistamines has made significant this adjuvant therapy.

Trimeton (prophenpyridamine) Maleate, an effective antihistamine, prepared in 0.5% aqueous solution for topical ophthalmic use, was used in a large number of external ocular allergies. Included were cases of conjunctivitis, dermatitis,

blepharoconjunctivitis, urticaria of the lids, and episcleritis, all of allergic origin.

Of twenty-three selected cases treated with Trimeton Maleate Ophthalmic Solution, 83% responded favorably. The only untoward reaction to the drug was a transient burning sensation.

Trimeton Maleate Solution, 0.5%, is recommended as topical adjuvant treatment in external ocular allergies.

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SIEGEL, IRVING *(Assoc. Prof. of Ob. and Gyn.).* Collection of Placental Blood, Amer. J. of Ob. and Gyn., Vol. 64, No. 6, pp. 1371-1373, Dec., 1952.

A technic of collecting placental blood is described which utilizes the apparatus commonly employed in collecting blood from donors in blood banks. Small bottles with a volume of 150 cc., containing ACD solution, and disposable sterile collecting tubes were utilized. Certain criteria for selecting placentas with the largest blood volumes are mentioned. The advantages of the technic described are: the blood is collected outside of the delivery room, the closed system of collection prevents contamination, the blood can be stored indefinitely, and a source of blood and blood fractions is suggested in view of the present shortage of blood and blood products.

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SIEGEL, IRVING *(Assoc. Prof. of Ob. and Gyn.).* Scars of the Pregnant and Non-Pregnant Uterus: I. Histologic Comparison of Scars Two Weeks Postoperatively, Amer. J. of Ob. and Gyn., Vol. 64, No. 2, pp. 301-308.

The author reviewed the literature pertaining to the effect of uterine scars on subsequent pregnancies. He compared histologically the healing of incisions made in the pregnant and non-pregnant uterus. His conclusion was that an incision into a pregnant uterus, e.g., cesarean section, heals with a greater production of connective tissue than an incision into the non-pregnant uterus, e.g., myomectomy. Thus, he believes that a patient who has had a myomectomy involving the uterine cavity should be treated in a subsequent pregnancy as if she had had a previous cesarean section. In other words, we should consider the possibility of uterine rupture during labor.

* * * * *

TAUB, SAMUEL J. *(Prof. of Med.).* Management of Seasonal Hay Fever, EENT Monthly, V. 30, No. 12, pp. 668-674, Dec., 1951.

The successful treatment of hay fever depends on the application of several principles. There is no known short cut method for the treatment of this ailment. Correct diagnosis is important in determining the etiological agent or agents responsible for symptoms. One of the most important steps in arriving at a diagnosis of seasonal hay fever is an accurate history containing the dates and places of onset of the initial symptoms. One should always inquire for dates which may furnish valuable clues as to the type of pollen responsible. For example, if a patient reported initial symptoms near Decoration Day, one would suspect tree pollens as the etiologic agent. Symptoms appearing around the Fourth of July would make grasses the likely cause, while an onset on Labor Day would implicate the ragweed group. The family history and past history must be obtained. A previous allergic manifestation on the part of the patient, such as eczema, hives, asthma, or food sensitivity may be disclosed and the existence of allergic disease in the patient's family may be revealed. The physical examination should be complete with particular attention being paid to the conjunctivae of the eyes, the nasal mucosa, turbinates, pharynx, and chest. The laboratory examination should include the usual blood and urine studies, nasal and ocular smears for eosinophiles, and complete intradermal skin tests. Treatment is divided into symptomatic, specific, or hyposensitization, coseasonal and perennial. ACTH and Cortisone are useful adjuvants in hay-fever complicated by asthma.

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WEYL, RUTH *(Assoc. Prof. Anesth.)*, WEI-CHI LIU, and EVELYN LIPP. Evaluation of the usefulness of intravenous sodium seconal in anesthesia, J. of the International College of Surgeons, 18:365-371, No. 3, September, 1952.

In this clinical study on 270 patients, seconal sodium in polyethylene glycol recently made available for intravenous use proved to be satisfactory as a hypnotic agent to supplement spinal anesthesia and as a basal anesthetic agent used prior to inhalation anesthesia. Administration is simple and induction of general anesthesia is pleasant. Sodium seconal is compatible with curare preparations and can be used with the main inhalation agents. In using it thus, it is important not to start any operative procedure before the patient is adequately saturated with the principal anesthetic agent. As anticipated, the potent agents, cyclopropane and ether, have to be used with good judgment to avoid respiratory depression and postoperative somnolence. The recommended technique is described in detail and variations and complications are discussed. Excellent masseter muscle relaxation was obtained in all cases. No increased vagal stimulation was noted and atraumatic easy intubation could be performed with the use of small amounts of curare. As with other barbiturates, hypotension may occur and the blood pressure has to be watched carefully. Injected intravenously, sodium seconal is a powerful hypnotic and respiratory depression or apnea may be produced by the drug alone, especially after preoperative sedation. It should be administered only when facilities for assisted respiration are available.

SCHOOL NOTES AND NEWS

PHI LAMBDA KAPPA HONORS SELIG

At their annual Senior Dinner-Dance on May 23, the Alpha Rho Chapter of the Phi Lambda Kappa Fraternity presented their second Annual Gold Medal Award for "loyal and devoted service to The Chicago Medical School" to Lester N. Selig, Chairman of the Board of Trustees of The Chicago Medical School since 1946.

(Photo by Scanlan)

In introducing Mr. Selig, President John J. Sheinin, first Annual Gold Medal recipient, stated that Mr. Selig was "primarily responsible for enlisting support and help from society for the school, enabling its students to become responsible and respected physicians."

Mr. Selig, Chairman of the Board of the General American Transportation Corporation, is also prominent for his active interest in social and educational fields, being Jewish Co-Chairman of the National Conference of Christians and Jews and a Trustee of the National Fund for Medical Education.

In accepting the award from Kenneth Cohen, Alpha Rho Chapter President, Mr. Selig stated sincerely that his work for The Chicago Medical School has been more than a worthwhile project and a vision fulfilled—it has been "fun." Mr. Selig and Dr. Sheinin hope to continue their work to make "a great school an even greater one."

FACULTY NEWS

Dean Francis J. Mullin has been named to the Medical Advisory Board of the Multiple Sclerosis Foundation of America.

Several Chicago Medical School faculty members participated in the program of the 113th Annual Meeting of the Illinois State Medical Society, held at the Hotel Sherman in Chicago, May 19-22. Papers were presented by Drs. Israel Davidsohn, Morris A. Kaplan, Kurt Stern, and Leo Zimmerman. Scientific exhibits were presented by Dr. E. D. Congdon, Dr. Hans Elias and John E. Pauly with Dr. Hans Popper of the Hektoen Institute, Drs. Piero P. Foa and Jay A. Smith, E. Magid, M. Glassman, and Miss Harriet Weinstein, Drs. J. Major and Earle I. Greene, Dr. Ceasar Portes, Drs. Manuel G. Spiesman and Louis Malow, and Drs. Leo Zimmerman and David H. Wagner.

Silver medals were awarded to Drs. Foa, Smith *et al* and Drs. Spiesman and Malow for meritorious exhibits. Dr. Congdon and Drs. Zimmerman and Wagner received bronze medals for their exhibits.

Department of Anatomy

Dr. Hans Elias, Assistant Professor of Microscopic Anatomy, has received two grants—one, renewal of a $4,000 grant from the National Heart Institute of the United States Public Health Service for

the study of "The Architecture of the Adrenal Cortex in Normal and Hypertensive Human Subjects," the other, an $11,600 grant for a period of two years for study of the "Morphology of Carcinoma of the Liver" from the National Cancer Institute of the United States Public Health Service.

Dr. Harold Koenig, Assistant Professor of Anatomy, has received a grant of $22,000 from the United States Public Health Service for research on "Morphologic and Quantitative Study of the Nucleoprotein in Living Cells Grown in Vitro and the Effect of Noxious Agents." This is a continuation of the work he has been doing with ultraviolet microspectroscopy.

Department of Medicine

Announcement has been made of the appointments of Dr. Louis Edidin as Assistant Professor of Clinical Medicine and Dr. Lloyd H. Grundset as Associate in Medicine. Drs. Harry F. Weisberg, Assistant Professor of Clinical Pathology, and Leonard A. Stine have been promoted to the positions of Assistant Professor of Clinical Medicine.

Dr. Aldo A. Luisada, Associate Professor of Medicine and Program Director of Cardiology, has received two grants: $9,700 from the Chicago Heart Association for study of Cardiac Murmurs, and $500 from the Chicago Heart Association to complete payment for new equipment.

Dr. Luisada has been appointed Associate Editor in Cardiology of *Diseases of the Chest,* official organ of the American College of Chest Physicians. He has also been confirmed as a member of the Rheumatic Fever Committee and the Research Committee of the Chicago Heart Association for 1953.

Department of Physiology

Friends of the late Dr. Howard Sloan have instituted a research grant of $500 per year for the benefit of the Department of Physiology of The Chicago Medical School. The grant is to be known as the Dr. Howard Sloan Memorial Research Grant.

Dr. Sloan, a 1942 alumnus of The Chicago Medical School, died June 15, 1952. He served at one time as Student Health Officer at the school and did research as a Fellow in the Department of Physiology. At the time of his death he was on leave of absence from the school, doing graduate work at the University of Chicago Medical School.

Dr. Ben B. Blivaiss, Assistant Professor of Physiology, has received a grant of $6,192 from the U.S.P.H.S. National Cancer Institute for the study of the "Mechanism of Experimental Induction and Inhibition of Testicular Tumors in Mice."

Department of Ophthalmology

Dr. Paul Hurwitz, Assistant Professor of Ophthalmology and member of the National Board of Governors of The Chicago Medical School, and Dr. Martha Rubin Folk, Assistant Professor of Ophthalmology, attended the annual meeting of the Pan-American Association of Ophthalmology which was held aboard the S.S. Italia during a ten-day cruise in the Caribbean. Dr. Hurwitz gave a paper on "The Use of Mechanical Refractors" and discussed a new type of operation for Glaucoma. Dr. Folk discussed "Diseases of the Lids."

Department of Surgery

Dr. Emanuel Marcus has been promoted to the position of Assistant Professor of Clinical Surgery.

Dr. Ulrico Sacchi has been appointed Research Assistant in Oncology. Dr. Sacchi is a graduate of the University of Genoa Medical School and is in this country as an exchange scholar by authority of the Department of State.

Dr. Philippe Shubik, Assistant Professor and Coordinator of Oncology, has received a Cancer Teaching Grant of $25,000 from the National Cancer Institute of the United States Public Health Service.

Department of Urology

The appointments of Dr. Irving J. Shapiro as Associate Professor of Urology and Dr. Herman M. Soloway as Associate Professor of Clinical Genito-Urinary Surgery have been announced.

Class of 1917

Colonel Carl B. Herrmann, M.C., U.S.-A.R. was Commanding Officer of the 5424th Induction Station until his retirement on June 13, 1953, after 36 years of reserve service. He was a Professor of Roentgenology at The Chicago Medical School and is a Past-President of the Medical Chapter Reserve Officers Association (1939).

Class of 1932

Best wishes to Dr. Frank J. Rojek, who has opened a new office at 2225 West North Avenue, Chicago, Illinois.

Class of 1943

Captain William O. Ackley (Assistant in Anatomy, on leave of absence) of Chicago, Illinois, has been graduated from the Medical Field Services School in the Korean Combat Zone. He has now been assigned to a unit in the United States Eighth Army.

Congratulations to Colonel Adio A. Freeman on his promotion to Brigadier General, Medical Corps, U.S.A.R. General Freeman is a Fellow of the American Psychiatric Association, a Diplomate of the American Board of Psychiatry and Neurology, and a Clinical Associate of the Los Angeles Psychoanalytic Institute. He has been active in reserve medical activities in Los Angeles since 1947.

Best wishes to Dr. Harold Zolan, who has opened a new office at 51 Bell Street, Hempstead, Long Island, New York.

Class of 1944

Captain Elmer S. Bellinger has returned to General Practice in Braidwood, Illinois. He has completed seven months in Sasebo, Japan, as Chief of the Medical Service and Laboratory Service at the United States Army Hospital there. He was awarded the Korean and United Nations Ribbons.

Class of 1945

Congratulations to Dr. and Mrs. Philip Porter on the birth of a son, Mitchell, on January 23, 1953.

Class of 1946

Dr. Louis J. Polskin has recently completed two years of active duty in the United States Army Medical Corps and has just reopened his office at 1401 South Florida Avenue, Lakeland, Florida. For more than half of his tour of duty, Dr. Polskin was a member of a medical-surgical team concerned with injuries produced by cold environment. For another period of time he was assigned to a research project devoted to nutrition and malaria.

Class of 1947

Dr. Lawrence E. Batlan completed a Residency in Radiology at Michael Reese Hospital in Chicago, Illinois, in December, 1952. He is now a First Lieutenant in Korea with the 121st Evacuation Hospital.

Dr. Abraham I. Feldman is a Resident in Obstetrics and Gynecology at Brooklyn Jewish Hospital, Brooklyn, N. Y.

Congratulations to Dr. Robert R. Simner upon his appointment as Clinical Instructor in Anesthesiology at Southwestern Medical School of the University of Texas, Galveston, Texas.

Class of 1948

First Lieutenants Morris Binder of Chicago, Illinois, and Melvyn Leichtling of Brooklyn, New York, are stationed at a prisoner of war camp in Korea and are attached to the 3rd Platoon of the 514th Medical Clearing Company.

Dr. William C. Feldman is a Resident in Obstetrics and Gynecology at Brooklyn Jewish Hospital, Brooklyn, New York.

Dr. Herbert Lipschutz has returned from Tokyo, Japan, and is awaiting his discharge from the Army.

Dr. Daniel G. Osman, formerly of Chicago, Illinois, has begun a Residency at Jackson Memorial Hospital, Miami, Florida. He recently returned from Korea where he served for two years as Captain and Chief Surgeon of his unit and was awarded the Bronze Star.

Congratulations to Dr. Carl Weiner upon his appointment as a Resident in Hematology at the Michael Reese Hospital in Chicago, Illinois. Dr. Weiner has completed two years of Residency in Internal Medicine at Cook County Hospital and Wesley Memorial Hospital in Chicago.

First Lieutenant Howard Wilk, formerly an anesthesiologist at Montefiore Hospital in Pittsburgh, Pennsylvania, was recently assigned to the 43rd Surgical Hospital in Korea, after having been graduated from the Medical Field Services Hospital, Fort Sam Houston, Texas.

Class of 1949

Congratulations to Dr. and Mrs. Bernard Kleppel on the birth of their daughter, Judy Beth, on March 28, 1953.

Dr. Edward Zucker has been discharged from military service after having been stationed in Tokyo, Japan.

Class of 1950

Congratulations to Dr. and Mrs. Herbert L. Fishbein on the birth of their son, Joseph Mark, on May 26, 1953. Dr. Fishbein presented two cases entitled, "A Rare Cause of Intussusception" and "Pre-sacral Neuroblastoma," before the Kings County Radiological Society on April 23, 1953.

First Lieutenant Tullio F. Tartaglia of New York City has been graduated from the Medical Field Services School in the Korean Combat Zone. He has now been assigned to a unit in the United States Eighth Army in Korea.

Best wishes to Dr. Joseph P. Vesce, who has opened an office at 8769 Fourteenth Avenue, Brooklyn, New York.

Class of 1951

Best wishes to Dr. and Mrs. Lawrence Berger on the birth of a daughter, Randy Ellen, on December 26, 1952.

Congratulations to Dr. Sanford Gaylord upon his appointment as Senior Assistant Resident in Internal Medicine at Mount Sinai Hospital, Cleveland, Ohio. Dr. Gaylord has spent the past year as a Clinical Instructor in Internal Medicine at Wayne University Medical School.

Congratulations to Dr. George J. Magid upon his appointment as Resident in Internal Medicine at Virginia Mason Hospital and Clinic, Seattle, Washington. Dr. Magid has been serving as Senior Assistant Surgeon, United States Public Health Service, Seattle, Washington.

Class of 1952

Congratulations to Dr. and Mrs. Robert Bragman on the birth of a boy, David Geoffrey, on May 17, 1953.

Congratulations to Dr. and Mrs. Stuart Cohn on the birth of their first daughter, Lora Joyce, on March 16, 1953.

Best wishes to Dr. Joseph Roshe and the former Miss June Kay Rosenfield on the occasion of their marriage on March 22, 1953.

Class of 1953

The recently graduated Class of 1953 held its Senior Dinner-Dance at the Bismarck Hotel on June 13th. Two faculty members, Dr. H. H. Garner and Dr. E. P. Leroy, were selected by the Class to be Guests of Honor for the evening. The hilariously pointed "show" put on by the class was enthusiastically received by all, including a large representation of the Faculty.

Congratulations to Dr. and Mrs. Marvin DeHaan on the birth of their first child, Mark Robert, on April 22, 1953.

Congratulations to Dr. and Mrs. Philip Jacoby on the birth of their fourth child, Douglas Frank, on June 10, 1953.

Best wishes to Dr. Walter Griesbach of Flushing, New York, and the former Miss Janet Simon of the Bronx, New York, on their marriage on June 21, 1953.

We wish to congratulate Dr. Jack Handel of New York City on his marriage to the former Miss Anita Kantar of Minneapolis, Minnesota, on June 27, 1953.

Best wishes to Dr. Donald Klotz of Fall River, Massachusetts, and the former Miss Jacqueline M. Cohen of Chicago, Illinois, on their marriage on June 27, 1953.

STUDENT NEWS

Class of 1954

Recent elections held by the members of the Junior class resulted as follows:
President .....Stanley Bauer
Vice-President .....Eugene Leibsohn
Secretary .....Saul L. Zimmerman
Treasurer .....Melvin Samuels
Student Council Representatives—
Theodore Feldman, Marvin Keller

Congratulations to Stanley and Shirley Bauer on the birth of their first child, Barbara Ellyn, on April 1, 1953.

We wish to congratulate Norman and Edythe Lovell on the birth of their first child, Bruce, on May 2, 1953.

Congratulations to Fred B. Cohen of Maplewood, New Jersey, and the former Miss Margarey Schneider of Forest Hills, New York, on their marriage on June 21, 1953.

Best wishes to Seymour Fishkin of Perth Amboy, New Jersey, and the former Miss Jacqueline Worobow of Chicago, Illinois, on the occasion of their marriage on June 21, 1953.

Class of 1955

The results of the recent elections held by the Sophomore class for officers for the year 1953-54 are as follows:
President ..... Melvin Greenblatt
Vice-President ..... Mortimer Lacher
Secretary-Treasurer —
Alicia Barach Schweiger
Student Council Representatives —
Edward Altchek, Stuart Eichenfield

Congratulations to Arthur Brandt of Brooklyn, New York, and the former Miss Anne Holmelund of Geneva, New York, on their marriage on June 28, 1953.

Best wishes to Melvin Goldzband of Chicago, Illinois, and the former Miss Marilyn Miller of Chicago, Illinois, on the occasion of their marriage on June 30, 1953.

Congratulations to Edward Altchek of the Bronx, New York, on his engagement to Miss Marilyn Pearl, also of the Bronx, New York.

Best wishes to Helmuth Stahlecker of Chicago, Illinois, on his engagement to Miss Vera Plesko, also of Chicago, Illinois. The wedding is planned for July 11, 1953.

Class of 1956

Recent elections held by the Freshman class for officers for the coming year resulted as follows:
President ..... Jerome Levitan
Vice-President ..... Sherwyn Warren
Secretary-Treasurer .. Marjorie Barnett
Student Council Representatives —
Murray Mazur, Harold Levine

Best wishes to Myles Marks of Hicksville, Long Island, and the former Miss Sandra Lomench of North Bellmore, Long Island, on their marriage on June 21, 1953.

Congratulations to Sanford Mossberg of Hartford, Conecticut, and the former Miss Phylsie Goldberg, also of Hartford, Connecticut, on their marriage on June 28, 1953.

ORGANIZATION NEWS

Student Council

Once again the annual Spring Dance, sponsored by the Student Council, was a gala success. The festivities this year were enhanced by the superb entertainment supplied by the Sophomore class. The presence of many faculty members served to increase the congeniality of the evening and allowed an opportunity for the students and their professors to meet socially.

As provided in the new Student Council constitution, elections were held in May. The officers of the Student Council for the coming year are: Edward Altchek, President; Theodore Feldman, Vice President; Maury Fields, Secretary; and Harold Levine, Treasurer.

Once again we are rapidly approaching a new academic year and, as always, the Student Council is busily preparing for the work which lies ahead. Part of our future program consists of Freshman orientation and housing programs.

Phi Lambda Kappa

On April 10, 1953, the Alpha Rho chapter of Phi Lambda Kappa continued its educational program by sponsoring the fourth in the series of Annual Maurice Oppenheim Memorial Lectures. Dr. Sid-

ney Farber, Director of the Children's Cancer Research Foundation of Boston, discussed "Diseases of Lipid Metabolism."

Elections were held on April 23, 1953, and the newly elected officers are: President, Eugene Trachtenberg; Vice-President, David Lipton; Secretary, Seymour Bradus; Treasurer, George Paul; Corresponding Secretary, Allen Bloom; Warden, Peter Brodney; Historian, Sheldon Waldman; and Student Council Representatives, Philip Mozer and Ronald Blatt.

Through the aid of frater Saul Zimmerman, PLK's film series reached a new peak when John Steinbeck's "The Forgotten Village" was presented for the enjoyment of the entire student body in the "Amph A Theater" on April 28th.

The annual Senior Dinner-Dance of Phi Lambda Kappa, held at the Furniture Club of America on Saturday evening, May 23, 1953, was highlighted by the presentation of the Second Annual Gold Medal Award to Mr. Lester N. Selig, Chairman of the Board of Trustees of The Chicago Medical School.

Phi Delta Epsilon

On March 10, 1953, the Phi Delta Epsilon fraternity met for the purpose of electing their new officers. The following members were chosen to guide the fraternity's activities for the coming year:

Consul ..... Norman Shapiro
Vice-Consul ..... David Tuman
Scribe ..... Jason Greenstein
Treasurer ..... Jerome Goldstein
Assistant Treasurer ..... Gerald Barron
Senior Senator ..... Fred B. Cohen
Junior Senator ..... Marvin Herz
Historian ..... Gerald Klebanoff

The members of the fraternity have full confidence in their new officers and it is felt that the coming year will be a fruitful one.

Association of Interns and Medical Students

The program for the Spring of this year consisted of a series of lectures concerned with acquainting the graduating student with the various pathways open to him after graduation. Among the speakers who participated in the program was Dr. Harold Koenig, who delivered a most informative talk on the relative merits of research versus medical practice.

These educational activities were well balanced by frequent social evenings at the homes of various members. The highlight of these social gatherings was the music of Maury and Nina Fields, both of whom are excellent guitarists.

The Fall program for A.I.M.S. was drawn up with the aid of our faculty advisors, Drs. Piero P. Foa and Peter Gaberman. The program will include the most stimulating lectures on medical and non-medical topics that are available.

A welfare committee was organized and is currently publishing a select list, based on student poll, of the best textbooks for every course given in the four-year curriculum. Another A.I.M.S. service currently available is a National Internship Survey.

Student American Medical Association

The Student American Medical Association of The Chicago Medical School opened its spring educational program by sponsoring the first in a series of lectures on "Progress in Endocrinology." It was a round table discussion on the Mechanism of Insulin Action, participated in by Drs. Sidney P. Colowick, Rachmiel Levine, and DeWitt Stetten. The second lecture was the first in a series entitled "Cancer Research—Today." Dr. Robert Schreck, Chief of Tumor Research at Hines Veterans Administration Hospital, discussed "Cell Death" and showed time-lapse motion pictures of cells undergoing degeneration. Other lectures included a discussion of "The Carbohydrate Metabolism of Tumor Tissue" by Dr. Ashman-Williams of the Ben May Cancer Hospital at the University of Chicago and a lecture on "The Fundamentals of Neuro-Psychiatry" by Dr. Jules H. Masserman, head of the Psychiatry Department of Northwestern Medical School.

Andrew Segal and Sheldon Waldman were appointed as representatives to the Student Council from S.A.M.A.

The following interneship appointments have been announced for the class of 1953:

Adler, Lawrence
Los Angeles County Hospital
Los Angeles 33, California

Arons, Ernest
Los Angeles County Hospital
Los Angeles 33, California

Bacher, Norman M.
Detroit Receiving Hospital
Detroit 26, Michigan

Bauer, Harry M.
Veterans Admin. Hospital
Long Beach 4, California

Behr, Donald J.
Queens General Hospital
Jamaica 32, New York

Berkowitz, Frederick
Veterans Admin. Hospital
Long Beach 4, California

Berkwits, Edward
Cook County Hospital
Chicago 12, Illinois

Bonn, Philip
Mississippi Baptist Hospital
Jackson, Mississippi

Breiner, Sander J.
The Grace Hospital
Detroit 1, Michigan

Buchwald, Julius
Kings County Hospital
Brooklyn 3, New York

Chazan, Solomon
Kings County Hospital
Brooklyn 3, New York

Cobrinik, Ralph W.
Meadowbrook Hospital
Hempstead, New York

Cohen, Ernest, Jr.
Michael Reese Hospital
Chicago 16, Illinois

Cohen, Kenneth D.
Einstein Med. Center, S.D.
Philadelphia 47, Pa.

Colburn, Daniel W.
City Hospital
Newark 7, New Jersey

DeHaan, Marvin R.
Cook County Hospital
Chicago 12, Illinois

Diamond, Edward
Newark Beth Israel Hospital
Newark 8, New Jersey

Esecover, Harold
Queens General Hospital
Jamaica 32, New York

Fagan, Lewis
Jackson Memorial Hospital
Miami 36, Florida

Fischer, Harold M.
City Hospital
Newark 7, New Jersey

Galef, Harold R.
U. S. P. H. S. Hospital
Staten Island, New York

Glickstein, Milton
The Mount Sinai Hospital
New York 29, New York

Gold, Jerome A.
Kings County Hospital
Brooklyn 3, New York

Gollub, Morton J.
Mount Sinai Hospital
Chicago 8, Illinois

Greenberg, Jesse D.
City Hospital
Newark 7, New Jersey

Greenberger, Alex M.
Beth El Hospital
Brooklyn 12, New York

Griesbach, Walter A.
Cincinnati General Hospital
Cincinnati 29, Ohio

Gussoff, Bernard D.
Cook County Hospital
Chicago 12, Illinois

Hammerschlag, Irving L.
Meadowbrook Hospital
Hempstead, New York

Handel, Jack E.
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Handler, Jerome L.
Cook County Hospital
Chicago 12, Illinois

Henning, Arthur J.
Los Angeles County Hospital
Los Angeles 33, California

Horning, John S.
Cook County Hospital
Chicago 12, Illinois

Jacobson, Lewis L.
Gallinger Municipal Hosp.
Washington 3, D. C.

Jacoby, Philip R.
Good Samaritan Hospital
Portland 10, Oregon

Jaffe, Stanley
Mount Sinai Hospital
Cleveland 6, Ohio

Jensen, Robert
Cook County Hospital
Chicago 12, Illinois

Jones, Clay H., Jr.
Cook County Hospital
Chicago 12, Illinois

Kessler, Samuel
Cook County Hospital
Chicago 12, Illinois

Klotz, Donald A.
Flushing Hosp. & Dispensary
Flushing 55, New York

Kranis, Marvin
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Kuvin, Seymour F.
Morristown Memorial Hosp.
Morristown, New Jersey

Langs, Robert J.
U. S. P. H. S. Hospital
Staten Island, New York

Lazar, Sanford H.
Cook County Hospital
Chicago 12, Illinois

Levit, Fred
Cook County Hospital
Chicago 12, Illinois

Lichtblau, Sheldon A.
Los Angeles County Hosp.
Los Angeles 33, California

Mason, Gene W.
Cook County Hospital
Chicago 12, Illinois

Miller, Irwin
Kings County Hospital
Brooklyn 3, New York

Pinchuck, Arthur L.
Maimonides Hospital
Brooklyn 19, New York

Rolnick, Donald T.
Michael Reese Hospital
Chicago 16, Illinois

Rubinstein, Martin J.
Mount Zion Hospital
San Francisco 15, Calif.

Rulin, Marvin C.
Cook County Hospital
Chicago 12, Illinois

Schiff, Melvin M.
Montefiore Hospital
Pittsburgh 13, Pennsylvania

Schneck, Larry
Kings County Hospital
Brooklyn 3, New York

Schoenfeld, Myron R.
Kings County Hospital
Brooklyn 3, New York

Schwab, Marilyn
Kings County Hospital
Brooklyn 3, New York

Shapiro, William H.
Mount Sinai Hospital
Cleveland 6, Ohio

Shatkin, Eugene P.
Alameda County Hospitals
Oakland 6, California

Solomon, Herschel H.
Kings County Hospital
Brooklyn 3, New York

Strick, Lawrence
Los Angeles County Hospital
Los Angeles 33, California

Sumner, Philip
Beth Israel Hospital
New York 3, New York

Telingator, Richard H.
U. S. P. H. S. Hospital
Staten Island, New York

Terrano, James V.
Ohio Valley General Hosp.
Wheeling, West Virginia

Tsumori, Himeo
Alameda County Hospitals
Oakland 6, California

Weiner, Gerald H.
Montefiore Hospital
Pittsburgh 13, Pennsylvania

Wildes, Jerome
Scranton State Hospital
Scranton 5, Pennsylvania

Winkler, Lesther H.
Montefiore Hospital
Pittsburgh 13, Pennsylvania

Ziffer, Herman
Cincinnati General Hospital
Cincinnati 29, Ohio

Zuckerman, Harvey S.
Beth El Hospital
Brooklyn 12, New York

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THE CHICAGO MEDICAL SCHOOL

QUARTERLY

710 South Wolcott Avenue
Chicago 12, Illinois

The Chicago Medical School *QUARTERLY* is published four times yearly by The Chicago Medical School for the dissemination of current medical news and for the advancement of medical science with a student staff under the supervision of a faculty editorial board.

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A minimum number of illustrations will be furnished by the *QUARTERLY* provided the photographs or drawings are of suitable quality.

Reprints will be furnished by the *QUARTERLY* without charge and must be requested when the manuscript is submitted.

Manuscripts for publication should be addressed to The Editor, The Chicago Medical School *QUARTERLY*, 710 S. Wolcott Avenue, Chicago 12, Illinois.

October issue deadline is August 1, 1953.

January issue deadline is November 1, 1953.

Bibliographies must conform in style to that used in *Quarterly Cumulative Index Medicus.*

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